

527, 500

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
1 April 2004 (01.04.2004)

PCT

(10) International Publication Number
WO 2004/027041 A2

(51) International Patent Classification⁷: C12N

(21) International Application Number:
PCT/US2003/029833

(22) International Filing Date:
18 September 2003 (18.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/412,327 19 September 2002 (19.09.2002) US
60/425,852 12 November 2002 (12.11.2002) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: *P. ARIASI* POLYPEPTIDES, *P. PERNICIOSUS* POLYPEPTIDES AND METHODS OF USE

(57) Abstract: Substantially purified salivary *P. ariasi* and *P. perniciosus* polypeptides, and polynucleotides encoding these polypeptides are disclosed. Vectors and host cells including the *P. ariasi* and *P. perniciosus* polynucleotides are also disclosed. In one embodiment, a method is disclosed for inducing an immune response to sand fly saliva. In other embodiments, methods for treating or preventing *Leishmaniasis* are disclosed.

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***P. ARIASI POLYPEPTIDES, P. PERNICIOSUS POLYPEPTIDES
AND METHODS OF USE***

5

PRIORITY CLAIM

This application claims the benefit of U.S. Provisional Application No. 60/412,327, filed September 19, 2002, and U.S. Provisional Application No. 60/425,852, filed November 12, 2002, which are incorporated herein by reference.

10

FIELD

The disclosure relates to proteins substantially purified from Phlebotomine sand fly salivary glands, or recombinant vectors expressing these proteins, and to an immune response produced to these proteins. This disclosure also relates to the production of an immune response that affects survival of Leishmania.

15

BACKGROUND

Leishmaniasis is a group of diseases caused by protozoa of the genus *Leishmania* that affects many millions of people worldwide. In humans, infection with the parasite manifests either as a cutaneous disease caused mainly by *L. major*, *L. tropica*, and *L. mexicana*; as a mucocutaneous disease caused mainly by *L. brasiliensis*; or as a visceral disease caused mainly by *L. donovani* and *L. chagasi*. In canids, *Leishmania* infections manifest as a visceral disease that can result in high death rates.

20

All leishmanial diseases are transmitted to their vertebrate hosts by phlebotomine sand flies, which acquire the pathogen by feeding on infected hosts and transmit them by regurgitating the parasite at the site of a subsequent blood meal (Killick-Kendrick, *Biology of Leishmania* in phlebotomine sand flies. *In Biology of the kinetoplastida*. W. Lumsden and D. Evans, editors. Academic Press, New York. 395, 1979).

25

While obtaining a blood meal, sand flies salivate into the host's skin. This saliva contains ant clotting, antiplatelet, and vasodilatory compounds that increase the hemorrhagic pool where sand flies feed (Ribeiro *et al.*, *Comp. Biochem. Physiol.* 4:683, 1986; Charlab *et al.*, *Proc. Natl. Acad. Sci. USA.* 26:15155, 1999). Some of

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these components are additionally immunomodulatory. For example, the New World sand fly *Lutzomyia longipalpis* contains the 6.5 kDa peptide, maxadilan, which is the most potent vasodilator known (Lerner *et al.*, *J. Biol. Chem.* 17:11234, 1991). Maxadilan additionally has immunosuppressive activities of its own
5 (Qureshi *et al.*, *Am. J. Trop. Med. Hyg.* 6:665, 1996), as do many persistent vasodilators such as prostaglandin E₂ (Makoul *et al.*, *J. Immunol.* 134:2645, 1985; Santoli and Zurier, *J. Immunol.* 143:1303, 1989; Stockman and Mumford, *Exp. Hematol.* 2:65, 1974) and calcitonin gene-related peptide (Nong *et al.*, *J. Immunol.* 1:45, 1989). Old World sand flies do not have maxadilan but instead use adenosine
10 monophosphate and adenosine as vasodilators (Ribeiro *et al.*, *J. Exp. Biol.* 11:1551, 1999). Adenosine is also an immunomodulatory component, promoting the production of interleukin-10 and suppressing tumor necrosis factor- α and interleukin-12 in mice (Hasko *et al.*, *J. Immunol.* 10:4634, 1996; Webster, *Asian Pac. J. Allergy Immunol.* 2:311, 1984; Hasko *et al.*, *FASEB J.* 14:2065, 2000).
15 Despite what is known about the role of sandfly saliva and disease transmission, much remains unknown, and an effective vaccine does not exist. Thus, there is a need for agents that can be used to induce an immune response to the organisms that cause leishmaniasis.

20

SUMMARY

The present disclosure relates to salivary proteins from sand fly vectors of *Leishmania* that are members of the subgenus of *Phlebotomus* Larroussius, in particular two species, namely *Phlebotomus ariasi* and *Phlebotomus perniciosus*, and the nucleic acids that encode these proteins. Methods of producing an immune
25 response in a subject are also disclosed.

Substantially purified salivary *P. ariasi* polypeptides are disclosed herein. Also disclosed are polynucleotides encoding the *P. ariasi* polypeptides disclosed herein.

Disclosed herein are substantially purified salivary *P. perniciosus*
30 polypeptides. Also disclosed are polynucleotides encoding the *P. perniciosus* polypeptides disclosed herein.

Methods are disclosed for inducing an immune response to a *P. ariasi* polypeptide using a therapeutically effective amount of the substantially purified salivary *P. ariasi* polypeptides disclosed herein, or the polynucleotides encoding the *P. ariasi* polypeptides disclosed herein.

5 Methods are also disclosed for inducing an immune response to a *P. perniciosus* polypeptide using a therapeutically effective amount of the *P. perniciosus* polypeptides disclosed herein, or the polynucleotides encoding the *P. perniciosus* polypeptides disclosed herein.

10 In another embodiment, methods are disclosed herein for inhibiting the symptoms of a *Leishmania* infection or for preventing a *Leishmania* infection in a subject. The methods include administering to the subject a therapeutically effective amount of a *P. ariasi* polypeptide, or a polynucleotide encoding a *P. ariasi* polypeptide.

15 In yet another embodiment, methods are disclosed herein for inhibiting the symptoms of a *Leishmania* infection or for preventing a *Leishmania* infection in a subject. The methods include administering to the subject a therapeutically effective amount of a *P. perniciosus* polypeptide, or a polynucleotide encoding a *P. perniciosus* polypeptide.

20 Pharmaceutical compositions are disclosed including a pharmaceutically acceptable carrier and a *P. ariasi* polypeptide and/or a *P. perniciosus* polypeptide.

The foregoing and other features and advantages will become more apparent from the following detailed description of several embodiments, which proceeds with reference to the accompanying figures.

25

SEQUENCE LISTING

30 The nucleic and amino acid sequences listed in the accompanying sequence listing are shown using standard letter abbreviations for nucleotide bases, and three letter code for amino acids, as defined in 37 C.F.R. 1.822. Only one strand of each nucleic acid sequence is shown, but the complementary strand is understood as included by any reference to the displayed strand. In the accompanying sequence listing:

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SEQ ID NO: 1 is the amino acid sequence of a PRL-P4-A10 polypeptide.

SEQ ID NO:2 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-A10 polypeptide.

SEQ ID NO: 3 is the amino acid sequence of PRL-P4-A9 polypeptide.

5 SEQ ID NO:4 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-A9 polypeptide.

SEQ ID NO:5 is the amino acid sequence of PRL-P4-C10 polypeptide.

SEQ ID NO:6 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-C10 polypeptide.

10 SEQ ID NO:7 is the amino acid sequence of PRL-P4-D6 polypeptide.

SEQ ID NO:8 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-D6 polypeptide.

SEQ ID NO:9 is the amino acid sequence of PRL-P4-D7 polypeptide.

15 SEQ ID NO:10 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-D7 polypeptide.

SEQ ID NO:11 is the amino acid sequence of PRL-P4-E5 polypeptide.

SEQ ID NO:12 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-E5 polypeptide.

SEQ ID NO:13 is the amino acid sequence of PRL-P4-F3 polypeptide.

20 SEQ ID NO:14 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-F3 polypeptide.

SEQ ID NO:15 is the amino acid sequence of PRL-P4-G12 polypeptide.

SEQ ID NO:16 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-G12 polypeptide.

25 SEQ ID NO:17 is the amino acid sequence of PRL-P4-G7 polypeptide.

SEQ ID NO:18 is the nucleic acid sequence of a polynucleotide encoding a PRL-P4-G7 polypeptide.

SEQ ID NO:19 is the amino acid sequence of PRL-P6-E11 polypeptide.

30 SEQ ID NO:20 is the nucleic acid sequence of a polynucleotide encoding a PRL-P6-E11 polypeptide.

SEQ ID NO:21 is the amino acid sequence of PRM-P3-A6 polypeptide.

SEQ ID NO:22 is the nucleic acid sequence of a polynucleotide encoding a PRM-P3-A6 polypeptide.

SEQ ID NO:23 is the amino acid sequence of PRM-P3-F11 polypeptide.

5 SEQ ID NO:24 is the nucleic acid sequence of a polynucleotide encoding a PRM-P3-F11 polypeptide.

SEQ ID NO:25 is the amino acid sequence of PRM-P5-D6 polypeptide.

SEQ ID NO:26 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-D6 polypeptide.

SEQ ID NO:27 is the amino acid sequence of PRM-P5-E9 polypeptide.

10 SEQ ID NO:28 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-E9 polypeptide.

SEQ ID NO:29 is the amino acid sequence of PRM-P5-F12 polypeptide.

SEQ ID NO:30 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-F12 polypeptide.

15 SEQ ID NO:31 is the amino acid sequence of PRM-P5-F2 polypeptide.

SEQ ID NO:32 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-F2 polypeptide.

SEQ ID NO:33 is the amino acid sequence of PRM-P5-G11 polypeptide.

20 SEQ ID NO:34 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-G11 polypeptide.

SEQ ID NO:35 is the amino acid sequence of PRM-P5-H4 polypeptide.

SEQ ID NO:36 is the nucleic acid sequence of a polynucleotide encoding a PRM-P5-H4 polypeptide.

SEQ ID NO:37 is the amino acid sequence of PRS-P1-B11 polypeptide.

25 SEQ ID NO:38 is the nucleic acid sequence of a polynucleotide encoding a PRS-P1-B11 polypeptide.

SEQ ID NO:39 is the amino acid sequence of PRS-P1-B4 polypeptide.

SEQ ID NO:40 is the nucleic acid sequence of a polynucleotide encoding a PRS-P1-B4 polypeptide.

30 SEQ ID NO:41 is the amino acid sequence of PRS-P1-E7 polypeptide.

SEQ ID NO:42 is the nucleic acid sequence of a polynucleotide encoding a PRS-P1-E7 polypeptide.

SEQ ID NO:43 is the amino acid sequence of PRS-P1-G9 polypeptide.

SEQ ID NO:44 is the nucleic acid sequence of a polynucleotide encoding a PRS-P1-G9 polypeptide.

SEQ ID NO:45 is the amino acid sequence of PRS-P2-C8 polypeptide.

5 SEQ ID NO:46 is the nucleic acid sequence of a polynucleotide encoding a PRS-P2-C8 polypeptide.

SEQ ID NO:47 is the amino acid sequence of PRS-P2-G8 polypeptide.

SEQ ID NO:48 is the nucleic acid sequence of a polynucleotide encoding a PRS-P2-G8 polypeptide.

10 SEQ ID NO:49 is the amino acid sequence of PERL-P7-G8 polypeptide.

SEQ ID NO:50 is the nucleic acid sequence of a polynucleotide encoding a PERL-P7-G8 polypeptide.

SEQ ID NO:51 is the amino acid sequence of PERL-P6-H9 polypeptide.

15 SEQ ID NO:52 is the nucleic acid sequence of a polynucleotide encoding a PERL-P6-H9 polypeptide.

SEQ ID NO:53 is the amino acid sequence of PERL-P7-C2 polypeptide.

SEQ ID NO:54 is the nucleic acid sequence of a polynucleotide encoding a PERL-P7-C2 polypeptide.

SEQ ID NO:55 is the amino acid sequence of PERL-P6-H1 polypeptide.

20 SEQ ID NO:56 is the nucleic acid sequence of a polynucleotide encoding a PERL-P6-H1 polypeptide.

SEQ ID NO:57 is the amino acid sequence of PERL-P3-E11 polypeptide.

SEQ ID NO:58 is the nucleic acid sequence of a polynucleotide encoding a PERL-P3-E11 polypeptide.

25 SEQ ID NO:59 is the amino acid sequence of PERL-P7-G12 polypeptide.

SEQ ID NO:60 is the nucleic acid sequence of a polynucleotide encoding a PERL-P7-G12 polypeptide.

SEQ ID NO:61 is the amino acid sequence of PERL-P3-C9 polypeptide.

30 SEQ ID NO:62 is the nucleic acid sequence of a polynucleotide encoding a PERL-P3-C9 polypeptide.

SEQ ID NO:63 is the amino acid sequence of PERM-P2-A10 polypeptide.

SEQ ID NO:64 is the nucleic acid sequence of a polynucleotide encoding a PERM-P2-A10 polypeptide.

SEQ ID NO:65 is the amino acid sequence of PERL-P6-H11 polypeptide.

5 SEQ ID NO:66 is the nucleic acid sequence of a polynucleotide encoding a PERL-P6-H11 polypeptide.

SEQ ID NO:67 is the amino acid sequence of PERS-P1-H11 polypeptide.

SEQ ID NO:68 is the nucleic acid sequence of a polynucleotide encoding a PERS-P1-H11 polypeptide.

SEQ ID NO:69 is the amino acid sequence of PERM-P2-G11 polypeptide.

10 SEQ ID NO:70 is the nucleic acid sequence of a polynucleotide encoding a PERM-P2-G11 polypeptide.

SEQ ID NO:71 is the amino acid sequence of PERM-P5-E2 polypeptide.

SEQ ID NO:72 is the nucleic acid sequence of a polynucleotide encoding a PERM-P5-E2 polypeptide.

15 SEQ ID NO:73 is the amino acid sequence of PERM-P5-C11 polypeptide.

SEQ ID NO:74 is the nucleic acid sequence of a polynucleotide encoding a PERM-P5-C11 polypeptide.

SEQ ID NO:75 is the amino acid sequence of PERM-P5-H8 (also referred to as P2-G9) polypeptide.

20 SEQ ID NO:76 is the nucleic acid sequence of a polynucleotide encoding a PERM-P5-H8 (also referred to as P2-G9) polypeptide.

SEQ ID NO:77 is the amino acid sequence of PERL-P3-B3 polypeptide.

SEQ ID NO:78 is the nucleic acid sequence of a polynucleotide encoding a PERL-P3-B3 polypeptide.

25 SEQ ID NO:79 is the amino acid sequence of PERM-P2-D11 polypeptide.

SEQ ID NO:80 is the nucleic acid sequence of a polynucleotide encoding a PERM-P2-D11 polypeptide.

SEQ ID NO:81 is the amino acid sequence of PERM-P5-E3 polypeptide.

30 SEQ ID NO:82 is the nucleic acid sequence of a polynucleotide encoding a PERM-P5-E3 polypeptide.

SEQ ID NO:83 is the amino acid sequence of PERM-P2-F11 polypeptide.

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SEQ ID NO:84 is the nucleic acid sequence of a polynucleotide encoding a PERM-P2-F11 polypeptide.

SEQ ID NO:85 is the nucleic acid sequence of the PT2F1 primer.

SEQ ID NO:86 is the nucleic acid sequence of the PT2R1 primer.

5 SEQ ID NO:87 is the nucleic acid sequence of the PT2F3 primer.

DETAILED DESCRIPTION

I. Abbreviations

10	AAV	adeno-associated virus
	AcNPV	Autographa California Nuclear Polyhedrosis Virus
	alum	aluminum phosphate or aluminum hydroxide
	BCG	Bacillus Calmette Guerin
15	BLAST	Basic Local Alignment Search Tool
	BSA	bovine serum albumin
	CAV	canine adenovirus
	CDR	complementarity determining region
	CHV	canine herpes virus
20	CMV	cytomegalovirus
	CTL	cytotoxic T lymphocyte
	DMRIE	N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanammonium
	DOPE	dioleoyl-phosphatidyl-ethanolamine
25	DTH	delayed type hypersensitivity
	fMLP	N-formyl-methionyl-leucyl-phenylalanine
	GM-CSF	granulocyte-macrophage colony stimulating factor
	H	heavy chains
	HLB	hydrophile-lipophile balance
30	ID	intradermal
	IM	intramuscular
	ISS	immunostimulating sequence
	KLH	keyhole limpet hemocyanin
	L	light chains
35	LB	Luria broth
	MVA	Modified Vaccinia virus Ankara
	ORF	open reading frame
	PCR	polymerase chain reaction
	polyA	polyadenylation signal
40	PVDF	polyvinylidene difluoride
	SC	subcutaneous
	SCA	Single chain antibody
	SDS-PAGE	sodium dodecyl sulfate-polyacrylamide gel electrophoresis
	sFv	single-chain antigen binding proteins
45	SGH	salivary gland homogenate

	SPGA	sucrose phosphate glutamate albumin
	tPA	tissue plasminogen activator
	V _H	variable region of the heavy chain
	V _L	variable region of the light chain
5	W/V	weight/volume

II. Terms

Unless otherwise noted, technical terms are used according to conventional usage. Definitions of common terms in molecular biology may be found in Benjamin Lewin, *Genes V*, published by Oxford University Press, 1994 (ISBN 0-19-854287-9); Kendrew *et al.* (eds.), *The Encyclopedia of Molecular Biology*, published by Blackwell Science Ltd., 1994 (ISBN 0-632-02182-9); and Robert A. Meyers (ed.), *Molecular Biology and Biotechnology: a Comprehensive Desk Reference*, published by VCH Publishers, Inc., 1995 (ISBN 1-56081-569-8).

In order to facilitate review of the various embodiments of the disclosure, the following explanations of specific terms are provided:

Amplification (of a nucleic acid molecule): A technique that increases the number of copies of a nucleic acid molecule (e.g., a DNA or an RNA) in a specimen. An example of amplification is the polymerase chain reaction, in which a biological sample collected from a subject is contacted with a pair of oligonucleotide primers, under conditions that allow for the hybridization of the primers to a nucleic acid template in the sample. The primers are extended under suitable conditions, dissociated from the template, and then re-annealed, extended, and dissociated to amplify the number of copies of the nucleic acid. The product of amplification may be characterized by electrophoresis, restriction endonuclease cleavage patterns, oligonucleotide hybridization or ligation, and/or nucleic acid sequencing using standard techniques. Other examples of amplification include strand displacement amplification, as disclosed in U.S. Patent No. 5,744,311; transcription-free isothermal amplification, as disclosed in U.S. Patent No. 6,033,881; repair chain reaction amplification, as disclosed in WO 90/01069; ligase chain reaction amplification, as disclosed in EP 0320308; gap filling ligase chain reaction amplification, as disclosed in 5,427,930; and NASBA™ RNA transcription-free amplification, as disclosed in U.S. Patent No. 6,025,134.

Antibody: immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen.

A naturally occurring antibody (*e.g.*, IgG, IgM, IgD) includes four
5 polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. However, it has been shown that the antigen-binding function of an antibody can be performed by fragments of a naturally occurring antibody. Thus, these antigen-binding fragments are also intended to be designated by the term "antibody." Specific, non-limiting examples of binding fragments encompassed
10 within the term antibody include (i) a Fab fragment consisting of the VL, VH, CL, and CH1 domains; (ii) an Fd fragment consisting of the VH and CH1 domains; (iii) an Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (iv) a dAb fragment (Ward *et al.*, *Nature* 341:544-546, 1989) which consists of a VH domain; (v) an isolated complementarity determining region
15 (CDR); and (vi) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region.

Immunoglobulins and certain variants thereof are known and many have been prepared in recombinant cell culture (*e.g.*, see U.S. Patent No. 4,745,055; U.S. Patent No. 4,444,487; WO 88/03565; EP 0256654; EP 0120694; EP 0125023;
20 Faoukner *et al.*, *Nature* 298:286, 1982; Morrison, *J. Immunol.* 123:793, 1979; Morrison *et al.*, *Ann Rev. Immunol* 2:239, 1984).

Animal: Living multi-cellular vertebrate organisms, a category that includes, for example, mammals and birds. The term mammal includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary
25 subjects, such as dogs.

Conservative variants: "Conservative" amino acid substitutions are those substitutions that do not substantially affect or decrease an activity or antigenicity of the *P. ariasi* or *P. perniciosus* polypeptide. Specific, non-limiting examples of a conservative substitution include the following examples:
30

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	Original Residue	Conservative Substitutions
5	Ala	Ser
	Arg	Lys
	Asn	Gln, His
	Asp	Glu
	Cys	Ser
10	Gln	Asn
	Glu	Asp
	His	Asn; Gln
	Ile	Leu, Val
	Leu	Ile; Val
15	Lys	Arg; Gln; Glu
	Met	Leu; Ile
	Phe	Met; Leu; Tyr
	Ser	Thr
	Thr	Ser
20	Trp	Tyr
	Tyr	Trp; Phe
	Val	Ile; Leu

The term conservative variation also includes the use of a substituted amino acid in place of an unsubstituted parent amino acid, provided that antibodies raised to the unsubstituted polypeptide also essentially immunoreact with the substituted polypeptide, or that an immune response can be generated against the substituted polypeptide that is similar to the immune response against the unsubstituted polypeptide. Thus, in one embodiment, non-conservative substitutions are those that reduce an activity or antigenicity.

cDNA (complementary DNA): A piece of DNA lacking internal, non-coding segments (introns) and expression control sequences. cDNA is synthesized in the laboratory by reverse transcription from messenger RNA extracted from cells.

Degenerate variant: A polynucleotide encoding a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide that includes a sequence that is degenerate as a result of the genetic code. There are 20 natural amino acids, most of which are specified by more than one codon. Therefore, all degenerate nucleotide sequences are included in the disclosure as long as the amino acid sequence of the *P. ariasi* polypeptide or *P. perniciosus* polypeptide encoded by the nucleotide sequence is unchanged.

Epitope: An antigenic determinant. These are particular chemical groups or peptide sequences on a molecule that are antigenic, *i.e.*, that elicit a specific immune response. An antibody specifically binds a particular antigenic epitope on a polypeptide. Specific, non-limiting examples of an epitope include a tetra- to penta-peptide sequence in a polypeptide, a tri- to penta-glycoside sequence in a polysaccharide. In the animal most antigens will present several or even many antigenic determinants simultaneously. Such a polypeptide may also be qualified as an immunogenic polypeptide and the epitope may be identified as described further.

Expression Control Sequences: Nucleic acid sequences that control and regulate the expression of a nucleic acid sequence, such as a heterologous nucleic acid sequence, to which it is operably linked. Expression control sequences are operably linked to a nucleic acid sequence when the expression control sequences control and regulate the transcription and, as appropriate, translation of the nucleic acid sequence. Thus expression control sequences can include appropriate promoters, enhancers, transcription terminators, polyA signals, a start codon (*i.e.*, ATG) in front of a protein-encoding polynucleotide sequence, splicing signal for introns, maintenance of the correct reading frame of that gene to permit proper translation of mRNA, and stop codons. The term "control sequences" is intended to include, at a minimum, components whose presence can influence expression, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences. Expression control sequences can include a promoter.

A promoter is a minimal sequence sufficient to direct transcription. Also included are those promoter elements which are sufficient to render promoter-dependent gene expression controllable for cell-type specific, tissue-specific, or inducible by external signals or agents; such elements may be located in the 5' or 3' regions of the gene. Both constitutive and inducible promoters, are included (see *e.g.*, Bitter *et al.*, *Methods in Enzymology* 153:516-544, 1987). For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage lambda, plac, ptrp, ptac (ptrp-lac-hybrid promoter) and the like may be used. In one embodiment, when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian

viruses (*e.g.*, the retrovirus long terminal repeat; the adenovirus late promoter; the vaccinia virus 7.5K promoter) can be used. Promoters produced by recombinant DNA or synthetic techniques may also be used to provide for transcription of the nucleic acid sequences. In one embodiment, the promoter is a cytomegalovirus promoter.

Host cells: Cells in which a vector can be propagated and its DNA expressed. The cell may be prokaryotic or eukaryotic. The term also includes any progeny of the subject host cell. It is understood that all progeny may not be identical to the parental cell since there may be mutations that occur during replication. However, such progeny are included when the term "host cell" is used. Also includes the cells of the subject.

Immune response: A response of a cell of the immune system, such as a B cell, T cell, or monocyte, to a stimulus. In one embodiment, the response is specific for a particular antigen (an "antigen-specific response"). The response can also be a non-specific response (not targeted specifically to salivary polypeptides) such as production of lymphokines. In one embodiment, an immune response is a T cell response, such as a CD4+ response or a CD8+ response. In another embodiment, the response is a B cell response, and results in the production of specific antibodies.

Immunogenic polypeptide: A polypeptide which comprises an allele-specific motif, an epitope or other sequence such that the polypeptide will induce an immune response. A specific, non-limiting example of an immune response includes binding an MHC molecule and inducing a cytotoxic T lymphocyte ("CTL") response, inducing a B cell response (*e.g.*, antibody production), and/or T-helper lymphocyte response, and/or a delayed type hypersensitivity (DTH) response against the antigen from which the immunogenic polypeptide is derived.

In one embodiment, immunogenic polypeptides are identified using sequence motifs or other methods known in the art. Typically, algorithms are used to determine the "binding threshold" of polypeptides to select those with scores that give them a high probability of binding at a certain affinity and will be immunogenic. The algorithms are based either on the effects on MHC binding of a particular amino acid at a particular position, the effects on antibody binding of a particular amino acid at a particular position, or the effects on binding of a particular

substitution in a motif- containing polypeptide. Within the context of an immunogenic polypeptide, a "conserved residue" is one which appears in a significantly higher frequency than would be expected by random distribution at a particular position in a polypeptide. In one embodiment, a conserved residue is one where the MHC structure may provide a contact point with the immunogenic polypeptide.

Immunogenic composition: A composition that, when administered to a subject, induces an immune response to a *Phlebotomus* salivary polypeptide. In one embodiment, the immune response is a positive DTH response.

Isolated: An "isolated" biological component (such as a nucleic acid or protein or organelle) has been substantially separated or purified away from other biological components in the cell of the organism in which the component naturally occurs, *i.e.*, other chromosomal and extra-chromosomal DNA and RNA, proteins, and organelles. Nucleic acids and proteins that have been "isolated" include nucleic acids and proteins purified by standard purification methods. The term also embraces nucleic acids and proteins prepared by recombinant technology as well as chemical synthesis.

Label: A detectable compound or composition that is conjugated directly or indirectly to another molecule to facilitate detection of that molecule. Specific, non-limiting examples of labels include fluorescent tags, enzymatic linkages, and radioactive isotopes.

Leishmaniasis: A parasitic disease spread by the bite of infected sand flies. The trypanosomatid parasite of the genus *Leishmania* is the etiological agent of a variety of disease manifestations, which are collectively known as leishmaniasis. Leishmaniasis is prevalent through out the tropical and sub-tropical regions of Africa, Asia, the Mediterranean, Southern Europe (old world), and South and Central America (new world). The old world species are transmitted by the sand fly vector *Phlebotomus sp.* Humans, wild animals and domestic animals (such as dogs) are known to be targets of these sandflies and to act as reservoir hosts or to develop leishmaniasis.

Cutaneous leishmaniasis starts as single or multiple nodules that develop into ulcers in the skin at the site of the bite. The chiclero ulcer typically appears as a

notch-like loss of tissue on the ear lobe. The incubation period ranges from days to months, even a year in some cases. The sores usually last months to a few years, with most cases healing on their own. The mucocutaneous type can develop into erosive lesions in the nose, mouth, or throat and can lead to severe disfigurement.

- 5 Visceral leishmaniasis often has fever occurring in a typical daily pattern, abdominal enlargement with pain, weakness, widespread swelling of lymph nodes, and weight loss, as well as superimposed infections because of a weakened immune system. Visceral leishmaniasis can result in high death rates. The onset of symptoms can be sudden, but more often tends to be insidious.

- 10 **Lymphocytes:** A type of white blood cell that is involved in the immune defenses of the body. There are two main types of lymphocytes: B cells and T cells.

Mammal: This term includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects.

- Oligonucleotide:** A linear polynucleotide sequence of up to about 100
15 nucleotide bases in length.

Open reading frame (ORF): A nucleic acid sequence having a series of nucleotide triplets (codons), starting with a start codon and ending with a stop codon, coding for amino acids without any internal termination codons. These sequences are usually translatable into a polypeptide.

- 20 **Operably linked:** A first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Generally, operably linked DNA
25 sequences are contiguous and, where necessary to join two protein-coding regions, in the same reading frame.

- Pharmaceutically acceptable vehicles or excipients:** The pharmaceutically acceptable vehicles or excipients of use are conventional. *Remington's Pharmaceutical Sciences*, by E. W. Martin, Mack Publishing Co., Easton, PA, 15th
30 Edition (1975), describes compositions and formulations suitable for pharmaceutical delivery of the polypeptides, plasmids, viral vectors herein disclosed.

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In general, the nature of the vehicle or excipient will depend on the particular mode of administration being employed. For instance, parenteral formulations usually comprise injectable fluids that include pharmaceutically and physiologically acceptable fluids such as water, physiological saline, balanced salt solutions, aqueous dextrose, glycerol or the like as a vehicle. For solid compositions (*e.g.*, freeze-dried pastille, powder, pill, tablet, or capsule forms), conventional non-toxic solid vehicles or excipients can include, for example, pharmaceutical grades of mannitol, lactose, starch, or magnesium stearate. In addition to biologically neutral vehicles or excipients, immunogenic compositions to be administered can contain minor amounts of non-toxic auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents and the like, for example sodium acetate or sorbitan monolaurate.

Phlebotomus ariasi (P. ariasi): A species of *Phlebotomus* (sand flies) genus endogenous to the Old World, in particular to southern Europe and Mediterranean countries, more particularly to Spain and France. This sand fly is a proven vector of visceral leishmaniasis. *P. ariasi* is a member of the subgenera of *Phlebotomus* Larroussius.

Phlebotomus perniciosus (P. perniciosus): A species of *Phlebotomus* (sand flies) genus endogenous to the Old World, in particular to southern Europe, and Mediterranean countries, more particularly to France, Italy, Greece, Morocco, and Spain. This sand fly is a proven vector of the visceral leishmaniasis. *P. perniciosus* is a member of the subgenera of *Phlebotomus* Larroussius.

Polynucleotide: The term polynucleotide or nucleic acid sequence refers to a polymeric form of nucleotide at least 10 bases in length, thus including oligonucleotides and genes. A recombinant polynucleotide includes a polynucleotide that is not immediately contiguous with both of the coding sequences with which it is immediately contiguous (one on the 5' end and one on the 3' end) in the naturally occurring genome of the organism from which it is derived. The term therefore includes, for example, a recombinant DNA which is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (*e.g.*, a cDNA) independent of other sequences. The polynucleotides can be ribonucleotides (*e.g.*

RNA), deoxyribonucleotides (e.g. DNA, cDNA), or modified forms of either nucleotide. The term includes single- and double-stranded forms of DNA.

Polypeptide: Any chain of amino acids, regardless of length (thus encompassing oligopeptides, peptides, and proteins) or post-translational
5 modification (e.g., glycosylation, phosphorylation, or acylation). A polypeptide encompasses also the precursor, as well as the mature polypeptide. In one embodiment, the polypeptide is a polypeptide isolated from *P. ariasi*, or encoded by a nucleic acid isolated from *P. ariasi*, such as the *P. ariasi* polypeptides disclosed herein. In another embodiment, the polypeptide is a polypeptide isolated from *P.*
10 *perniciosus*, or encoded by a nucleic acid isolated from *P. perniciosus*, such as the *P. perniciosus* polypeptides disclosed herein.

Fusion proteins are encompassed by the term polypeptide. Fusion proteins have at least two domains of two different polypeptides fused together. In one embodiment, one domain is a detectable label. The two domains of a fusion protein
15 can be genetically fused together, for instance directly or through the use of a linker oligonucleotide, thereby producing a single fusion-encoding nucleic acid molecule. The translated product of such a fusion-encoding nucleic acid molecule is a fusion protein. In one embodiment, one domain of the fusion protein is a *P. ariasi* or a *P. perniciosus* polypeptide and another domain of the fusion protein is a detectable
20 label. The detectable label can be green fluorescent protein, a myc tag or a histidine tag, or the like.

Polypeptide Modifications: *P. ariasi* polypeptides or *P. perniciosus* polypeptides include synthetic embodiments of polypeptides described herein. In addition, analogues (non-peptide organic molecules), derivatives (chemically
25 functionalized peptide molecules obtained starting with the disclosed polypeptide sequences) and variants (homologs) of these proteins can be utilized in the methods described herein. Each polypeptide of the disclosure is comprised of a sequence of amino acids, which may be either L- and/or D- amino acids, naturally occurring and otherwise.

30 Polypeptides may be modified by a variety of chemical techniques to produce derivatives having essentially the same activity as the unmodified polypeptides, and optionally having other desirable properties. For example,

carboxylic acid groups of the protein, whether carboxyl-terminal or side chain, may be provided in the form of a salt of a pharmaceutically-acceptable cation or esterified to form a C₁-C₁₆ ester, or converted to an amide of formula NR₁R₂ wherein R₁ and R₂ are each independently H or C₁-C₁₆ alkyl, or combined to form a heterocyclic ring, such as a 5- or 6- membered ring. Amino groups of the peptide, whether amino-terminal or side chain, may be in the form of a pharmaceutically-acceptable acid addition salt, such as the HCl, HBr, acetic, benzoic, toluene sulfonic, maleic, tartaric, and other organic salts, or may be modified to C₁-C₁₆ alkyl or dialkyl amino or further converted to an amide.

Hydroxyl groups of the peptide side chains may be converted to C₁-C₁₆ alkoxy or to a C₁-C₁₆ ester using well-recognized techniques. Phenyl and phenolic rings of the peptide side chains may be substituted with one or more halogen atoms, such as fluorine, chlorine, bromine, or iodine, or with C₁-C₁₆ alkyl, C₁-C₁₆ alkoxy, carboxylic acids and esters thereof, or amides of such carboxylic acids. Methylene groups of the peptide side chains can be extended to homologous C₂-C₄ alkylenes. Thiols can be protected with any one of a number of well-recognized protecting groups, such as acetamide groups. Those skilled in the art will also recognize methods for introducing cyclic structures into the peptides of this disclosure to select and provide conformational constraints to the structure that result in enhanced stability.

Peptidomimetic and organomimetic embodiments are envisioned, whereby the three-dimensional arrangement of the chemical constituents of such peptido- and organomimetics mimic the three-dimensional arrangement of the peptide backbone and component amino acid side chains, resulting in such peptido- and organomimetics of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide having measurable or enhanced ability to generate an immune response. For computer modeling applications, a pharmacophore is an idealized, three-dimensional definition of the structural requirements for biological activity. Peptido- and organomimetics can be designed to fit each pharmacophore with current computer modeling software (using computer assisted drug design or CADD). See Walters, "Computer-Assisted Modeling of Drugs," Klegerman & Groves (eds.), 1993, *Pharmaceutical Biotechnology*, Interpharm Press: Buffalo Grove, IL, pp. 165-174

and *Principles of Pharmacology* Munson (ed.) 1995, Ch. 102, for descriptions of techniques used in CADD. Also included are mimetics prepared using such techniques.

Probes and primers: A probe comprises an isolated polynucleotide
5 attached to a detectable label or reporter molecule. Primers are short polynucleotides. In one embodiment, polynucleotides are 15 nucleotides or more in length. Primers may be annealed to a complementary target DNA strand by nucleic acid hybridization to form a hybrid between the primer and the target DNA strand, and then extended along the target DNA strand by a DNA polymerase enzyme.
10 Primer pairs can be used for amplification of a nucleic acid sequence, *e.g.*, by the polymerase chain reaction (PCR) or other nucleic-acid amplification methods known in the art. One of skill in the art will appreciate that the specificity of a particular probe or primer increases with its length. Thus, for example, a primer comprising 20 consecutive nucleotides will anneal to a target with a higher specificity than a
15 corresponding primer of only 15 nucleotides. Thus, in order to obtain greater specificity, probes and primers may be selected that comprise at least 15, 20, 25, 30, 35, 40, 50 or more consecutive nucleotides.

Promoter: A promoter is an array of nucleic acid control sequences that directs transcription of a nucleic acid. A promoter includes necessary nucleic acid
20 sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements which can be located as much as several thousand base pairs from the start site of transcription. Both constitutive and inducible promoters are included (see *e.g.*, Bitter *et al.*, *Methods in Enzymology* 153:516-544,
25 1987). Promoters may be cell-type specific or tissue specific.

Specific, non-limiting examples of promoters include promoters derived from the genome of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the retrovirus long terminal repeat; the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used. Promoters produced by
30 recombinant DNA or synthetic techniques may also be used. A polynucleotide can be inserted into an expression vector that contains a promoter sequence which facilitates the efficient transcription of the inserted genetic sequence of the host.

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The expression vector typically contains an origin of replication, a promoter, as well as specific nucleic acid sequences that allow phenotypic selection of the transformed cells.

Protein Purification: The *P. ariasi* polypeptides and *P. perniciosus* polypeptides disclosed herein can be purified by any of the means known in the art. See, e.g., *Guide to Protein Purification*, Deutscher (ed.), *Meth. Enzymol.* 185, Academic Press, San Diego, 1990; and Scopes, *Protein Purification: Principles and Practice*, Springer Verlag, New York, 1982. Substantial purification denotes purification from other proteins or cellular components. A substantially purified protein is at least 60%, 70%, 80%, 90%, 95%, or 98% pure. Thus, in one specific, non-limiting example, a substantially purified protein is 90% free of other proteins or cellular components.

Purified: The term purified does not require absolute purity; rather, it is intended as a relative term. Thus, for example, a purified polypeptide preparation is one in which the polypeptide is more enriched than the polypeptide is in its natural environment. A polypeptide preparation is substantially purified such that the polypeptide represents, in several embodiments, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 99%, of the total polypeptide content of the preparation. The same applies for polynucleotides. The polypeptides disclosed herein can be purified by any of the means known in the art (see, e.g., *Guide to Protein Purification*, Deutscher (ed.), *Meth. Enzymol.* 185, Academic Press, San Diego, 1990; and Scopes, *Protein Purification: Principles and Practice*, Springer Verlag, New York, 1982).

Recombinant: A recombinant polynucleotide is one that has a sequence that is not naturally occurring or has a sequence that is made by an artificial combination of two otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques.

Selectively hybridize: Hybridization under moderately or highly stringent conditions that excludes non-related nucleotide sequences.

In nucleic acid hybridization reactions, the conditions used to achieve a particular level of stringency will vary, depending on the nature of the nucleic acids being hybridized. For example, the length, degree of complementarity, nucleotide sequence composition (*e.g.*, GC v. AT content), and nucleic acid type (*e.g.*, RNA v. DNA) of the hybridizing regions of the nucleic acids can be considered in selecting hybridization conditions. An additional consideration is whether one of the nucleic acids is immobilized, for example, on a filter.

A specific, non-limiting example of progressively higher stringency conditions is as follows: 2 x SSC/0.1% SDS at about room temperature (hybridization conditions); 0.2 x SSC/0.1% SDS at about room temperature (low stringency conditions); 0.2 x SSC/0.1% SDS at about 42°C (moderate stringency conditions); and 0.1 x SSC at about 68°C (high stringency conditions). One of skill in the art can readily determine variations on these conditions (*e.g.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., vol. 1-3, ed. Sambrook *et al.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). Washing can be carried out using only one of these conditions, *e.g.*, high stringency conditions, or each of the conditions can be used, *e.g.*, for 10-15 minutes each, in the order listed above, repeating any or all of the steps listed. However, as mentioned above, optimal conditions will vary, depending on the particular hybridization reaction involved, and can be determined empirically.

Sequence identity: The similarity between amino acid sequences is expressed in terms of the percentage identity between the sequences. The higher the percentage, the more similar the two sequences are. Homologs or variants of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide will possess a significant degree of sequence identity when aligned using standard methods.

Methods of alignment of sequences for comparison are well known in the art. Various programs and alignment algorithms are described in: Smith and Waterman, *Adv. Appl. Math.* 2:482, 1981; Needleman and Wunsch, *J. Mol. Biol.* 48:443, 1970; Pearson and Lipman, *Proc. Natl. Acad. Sci. U.S.A.* 85:2444, 1988; Higgins and Sharp, *Gene* 73:237, 1988; Higgins and Sharp, *CABIOS* 5:151, 1989; Corpet *et al.*, *Nucleic Acids Research* 16:10881, 1988; and Pearson and Lipman, *Proc. Natl. Acad. Sci.*

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U.S.A. 85:2444, 1988. Altschul *et al.*, *Nature Genet.*, 6:119, 1994 presents a detailed consideration of sequence alignment methods and identity calculations.

The NCBI Basic Local Alignment Search Tool (BLAST) (Altschul *et al.*, *J. Mol. Biol.* 215:403, 1990) is available from several sources, including the National
5 Center for Biotechnology Information (NCBI, Bethesda, MD) and on the Internet, for use in connection with the sequence analysis programs blastp, blastn, blastx, tblastn, and tblastx. A description of how to determine sequence identity using this program is available on the NCBI website on the internet.

Homologs and variants of a *P. ariasi* polypeptide or a *P. perniciosus*
10 polypeptide are typically characterized by possession of at least 75%, for example at least 80%, sequence identity counted over the full length alignment with the amino acid sequence of the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide using the NCBI Blast 2.0, gapped blastp set to default parameters. The comparison between the sequences is made over the full length alignment with the amino acid sequence given
15 in this present disclosure, employing the Blast 2 sequences function using the default BLOSUM62 matrix set to default parameters, (gap existence cost of 11, and a per residue gap cost of 1).

When aligning short peptides (fewer than around 30 amino acids), the alignment should be performed using the Blast 2 sequences function, employing the
20 PAM30 matrix set to default parameters (open gap 9, extension gap 1 penalties). Proteins with even greater similarity to the reference sequences will show increasing percentage identities when assessed by this method, such as at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% sequence identity. When less than the entire sequence is being compared for sequence identity, homologues and,
25 variants will typically possess at least 80% sequence identity over short windows of 10-20 amino acids, and may possess sequence identities of at least 85% or at least 90% or 95% depending on their similarity to the reference sequence. Methods for determining sequence identity over such short windows are available at the NCBI website on the internet. One of skill in the art will appreciate that these sequence
30 identity ranges are provided for guidance only; it is entirely possible that strongly significant homologues could be obtained that fall outside of the ranges provided.

Specific binding agent: An agent that binds substantially only to a defined target. Thus a *P. ariasi* specific binding agent is an agent that binds substantially to a *P. ariasi* polypeptide. Similarly, a *P. perniciosus* specific binding agent is an agent that binds substantially to a *P. perniciosus* polypeptide.

5 In one embodiment, the specific binding agent is a monoclonal or polyclonal antibody that specifically binds the *P. ariasi* polypeptide. In another embodiment, the specific binding agent is a monoclonal or polyclonal antibody that specifically binds the *P. perniciosus* polypeptide.

10 **Subject:** Living multi-cellular vertebrate organisms, a category that includes both human veterinary subjects, including human and non-human mammals. In one embodiment, the subject is a member of the canine family, such as a dog. In another embodiment, the subject is a human.

15 **T Cell:** A white blood cell critical to the immune response. T cells include, but are not limited to, CD4⁺ T cells and CD8⁺ T cells. A CD4⁺ T lymphocyte is an immune cell that carries a marker on its surface known as "cluster of differentiation 4" (CD4). These cells, also known as helper T cells, help orchestrate the immune response, including antibody responses as well as killer T cell responses. CD8⁺ T cells carry the "cluster of differentiation 8" (CD8) marker. In one embodiment, a CD8 T cells is a cytotoxic T lymphocytes. In another embodiment, a CD8 cell is a suppressor T cell.

20 **Therapeutically active polypeptide:** An agent, such as a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide, that causes induction of an immune response, as measured by clinical response (for example, increase in a population of immune cells, production of antibody that specifically binds the *P. ariasi* polypeptide or *P. perniciosus* polypeptide, a measurable reduction in symptoms resulting from exposure to *Leishmania*,
25 or protection from infection with *Leishmania*). Therapeutically active molecules can also be made from nucleic acids. Examples of a nucleic acid based therapeutically active molecule is a nucleic acid sequence that encodes a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide, wherein the nucleic acid sequence is operably linked to a control element such as a promoter. Therapeutically active agents can also include organic or
30 other chemical compounds that mimic the effects of the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide.

The terms "therapeutically effective fragment of a *P. ariasi* polypeptide" or "therapeutically effective variant of a *P. ariasi* polypeptide" includes any fragment of the *P. ariasi* polypeptide, or variant of the *P. ariasi* polypeptide, that retains a function of the *P. ariasi* polypeptide, or retains an antigenic epitope of the *P. ariasi* polypeptide, or retains the ability to reduce the symptoms from exposure to *Leishmania*, or to protect from infection with *Leishmania*. The terms "therapeutically effective fragment of a *P. perniciosus* polypeptide" or "therapeutically effective variant of a *P. perniciosus* polypeptide" includes any fragment of the *P. perniciosus* polypeptide, or variant of the *P. perniciosus* peptide, that retains a function of the *P. perniciosus* polypeptide, or retains the ability to reduce the symptoms from exposure to *Leishmania*, or to protect from infection with *Leishmania*.

Thus, in one embodiment, a therapeutically effective amount of a fragment of *P. ariasi* polypeptide or a *P. perniciosus* polypeptide is an amount used to generate an immune response to the polypeptide. In another embodiment, a therapeutically effective amount of a fragment of *P. ariasi* polypeptide or a *P. perniciosus* polypeptide is an amount of use to prevent or treat a *Leishmania* infection in a subject. Treatment refers to a therapeutic intervention that confers resistance to infection with *Leishmania*, or a reduction in the symptoms associated with exposure to *Leishmania*. Specific, non-limiting examples of a polypeptide fragment are the N-terminal half or the C-terminal half of one of the *P. ariasi* polypeptides or the *P. perniciosus* polypeptide disclosed herein.

Transduced: A transduced cell is a cell into which has been introduced a nucleic acid molecule by molecular biology techniques. As used herein, the term transduction encompasses all techniques by which a nucleic acid molecule might be introduced into such a cell, including transfection with viral vectors, transformation with plasmid vectors, and introduction of naked DNA by electroporation, lipofection, and particle gun acceleration.

Vaccine: Composition that when administered to a subject, induces a decrease of the severity of the symptoms of a disorder or disease. In one embodiment, a vaccine decreases the severity of the symptoms of leishmaniasis and/or decreases the parasitic load.

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Vector: A nucleic acid molecule as introduced into a host cell, thereby producing a transduced host cell. A vector may include nucleic acid sequences that permit it to replicate in a host cell, such as an origin of replication. A vector may also include one or more selectable marker genes and other genetic elements known
5 in the art.

Unless otherwise explained, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art
10 to which this disclosure belongs. The singular terms "a," "an," and "the" include plural referents unless context clearly indicates otherwise. Similarly, the word "or" is intended to include "and" unless the context clearly indicates otherwise. "Comprise" means "include," and a composition that comprises a polypeptide includes that polypeptide. It is further to be understood that all base sizes or amino
15 acid sizes, and all molecular weight or molecular mass values, given for polynucleotides or polypeptides are approximate, and are provided for description. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and
20 other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including explanations of terms, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

25

***P. ariasi* and *P. perniciosus* Polynucleotides and Polypeptides**

Salivary polypeptides from sand fly species of the subgenera of *Phlebotomus* Larroussius, in particular *P. ariasi* and *P. perniciosus*, are disclosed herein. *P. ariasi* polypeptides include polypeptides having a sequence as set forth as SEQ ID
30 NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31,

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SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47, and conservative variants thereof.

Specific, non-limiting examples of an amino acid sequence of a *P. ariasi* polypeptide are set forth below:

5 PRL-P4-A10 (SEQ ID NO:1)

MKLVPLCILVCFLIAQQVAQNEASPAKSQDAMYGDWSRWSSCDEATCHQTK
VRSCLGAVCERNRLMKERKCPGCGTKVRIVQKLLQLFGMGDSIETDYEDDY
GEHWLTDDRVISSRNDPESAESDELGSFFRDFHSDFEWKNPFSNPHENND
VDLEVEEDEEVEELPEIRTSNEEDSVSGADHVCVGTKNERSSGMMAKTIGG
10 RNSKKGRWPWQVALYNQEYENFFCGGTLISKYWVITAAHCLISDFGSDITIF
SGLYDTGDLVESPYSIHLVRDRVIHPRYDAETNDNDIALRLYNEVKLSDDV
GIACLPSSYSQASPRSEVCKVLGWGQGTRRTKLQEADMHIQPANSCKRHYY
GTGQLVTRHMLCASSRNYVSDTCGGDSGGPLLCDTKSPARPWTFLFGITSF
GDDCTVSESPGVYARVASFRKWIDSVIECDGSCDN

15

PRL-P4-A9 (SEQ ID NO:3)

MNILLKVAILVSLCEIGYSWKYPRNADQTLWAWRSCQKGNYPDELVKKW
MAFEIPDDEVTHCYIKCVWTHLGMYDETSQTRADRVKQQFKARGLSVPAE
ISHLEGSTGGSCVTIYKKTRAFLETQMPNYRIAFYGTVEESDKWFANNPETK
20 PKRIKISDFCKGREAGTEGTCKHACSMYYYRLVDEDNLVIPFRKLPGILDSQ
LEQCRDQASSETGCKVGDTIYNCLNRINPEGLKKALNTLDEQSLTLY

PRL-P4-C10 (SEQ ID NO:5)

MKIFLCLFAAVSIQGALASQIEREYAWKNIYEGIDQGSYNIENSIPTAFAHDA
25 ASKKIFITIPRINQVPITLTEFDSIKYPGGSPPLSKFPGSDNIISVYQPVIDECRRL
WIVDAGQVEYKGDEQKYPKKNPAILAYDLTKDNYPEIDRYEIPINIAGNPLGF
GGFTVDVTNPKEGCGKTFIYITNFEDNTLIVYDQEKKDSWKISHGSFKPEHES
ILIHNGVDHILKLGIFGITLGDRDSEGNRPAYYLGGSSTKLFEVNTKALKKKE
GEIEPITLGDRGPHSEALALAYDPKTKVIFFTYNSKKISCWNKKPLIHDNMD
30 KIYASPEFIFGTDISVDSSEKLVFFSNGHPPIENLQLSSDKPHIHLISVDTEKAI
RGTKCEVKA

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PRL-P4-D6 (SEQ ID NO:7)

MKIFMGLIAVVS LQ GALAYHVEREYAWKNITFEGIDQASYNIENSIPTAFVH
DALSKKIIIAIPRLYPQVPITLTQLDTTKHPERSPPLEKFP GSDKLT SVYQPML
DECRRLLWIVDVGQVEYKGDEQKYPKKNPAILAYDLTKDNYPEIDRYEIPINIA
5 GNQIGFGGFTVDVTNPKEGCGKTFIYITNFEDNTLIVYDQEKKDSWKISHGSF
KPEHESNFSHNGAQYKYKAGIFGITLGDRDPEGNRPAYYLGGSSSTKLFEVST
EALKKKKGAKFDPVRLGDRGRHTEAIALVYDPKTKVIFFAESDSRQISCWNTQ
KPLNHNKNTDVIIYASSKFIFGTDIQIDSDSQLWFLSNGQPPIDNLKLTFDKPHIR
LMRVDTKNSIRRTCEVKPIKKP

10

PRL-P4-D7 (SEQ ID NO:9)

MFKEIIVVALAVIVAQCAPPAPIAKQGNDFPVPIVDEKETDDFFDDRFPDID
DERVGARAPVGGKQTSNRGTSSQSDKVPRPQGSNRGPSSQTTDKVPRPQWP
SRGTNSQNDKVPRPQGSSGQTPPRTPGKVEQSGRTNTKDQIPRPLTNRNPTK
15 NPTEQARRPGNRELLIRDKTPGSQGGKQGTGNRQKLSSYKDAQPKLIFKSSQ
FNTDGGQNPYLTRLFKTKKVEEVIAKGSPTDEYVLELLDGKPDNLSLVIRTNG
KTSQAVLRNPTRNRIVGRIKSYNPGPRRMSY

PRL-P4-E5 (SEQ ID NO:11)

20 MASIKLSTCSFVLLNLILPTISMKVISFDDRDEYLLGKPANSDDELLYSTFDFQ
RDPCSKSYVKCTNNNTHFILDFVDPKKRCISSIHVFSYPDRPPSFEEKRIPSKS
AIYCQKGGIGKSHCLLVFRKKEPREDALVDIRGIPADQTC SLKERYTSGDPK
KTDAYGMAYQFDRKDDWHIQR TGIKTWKRSGNEIFYRKNGLMNHQIRYLS
KFDKYTVTREL VVKNNAKKFTLEFSNFRQYRISFLDIYWFQESQRNKPRLPY
25 IYYNGHCLPSNKTCQLVFDTDEPITYAFVKVFSNPDHNEPRLRHEDLGRG

PRL-P4-F3 (SEQ ID NO:13)

MVIYLTQNISRALLTLLPNPEDVRSAAADVLESFTDDLKSFYPPDDVNEEVSE
TESRTKRSLIEQLKESQPLKQIRETVAETTKYLGFLKTKPSGNQTESSNSTST
30 KTQSRKRRGLTDFIPVNSLKDAISQATSGAMKAFKPSSENKTSSNPLDFLASL
SDISRDLVQNSIKEVSGNLVSSVALYQVNSKLDAIKQSIGINQEIDRTKKVQ
QYVMNALQQASNITNSIGEQLKSNNCFAQFINPFKLFEEVITCVKNKIENGLK

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IAETFKNLNQALSVPSDIVSEVSKCSQNQNLNPLTKLLCYLRVPLQLDEEKL
LLPIEFARRIREITNYFATMRMDLIQCGIATIQSIGDKVENCAIEAILAVKDTL
KG

5 PRL-P4-G12 (SEQ ID NO:15)

MKQFPVILLTLGLLVVKCRSERPEWK CERDFKKIDQNCFRPCTFAIYHFVDN
KFRIARKNIENYKKFLIDYNTVKPEVNDLEKHLLDCWNTIKSIEASSRTEKCE
QVNNFERCVIDKNILNYPVYFNALKKINKNTNV

10 PRL-P4-G7 (SEQ ID NO:17)

MINPIVLRFTFLLVILLPGKCKSAPKSCTINLPTSIPKKGEPIYLSNNGSVFRPIG
GLTQLNIGDSL SIYCPPLKKLKSVPKSRKFSLESYSCNNSQSELVQTEEECG
QEGKWYNIGFPLPTNAFHTIYRTCFNKQKLTPIYSYH VINGKAVGYHVKQPR
GNFRPGKGVYRKININELYKTHISRFKKVFGDKQTFFRKPLHYLARGHLSPE
15 VDFVFGTEQHATEFYINTAPQYQSINQGNWLRVEKHVRGLAKALQDNLLV
VTGILDILKFSNKRADTEIYLG DG IIPVPQIFWKAIFHLRTSSAIVFVTSNNPHE
TTFNNICKDACEMAGFGDKQHGNQNF SNYSLGFTICCELQDFIGNSKVVLPK
DIQVKNHRKLLQLPKPKQ

20 PRL-P6-E11 (SEQ ID NO:19)

MNALLCVLLSLSGIGYSWKYPRNADQTLWAYRTCQREGKDPALVSKWM
NWVLPDDPETHCYVKCVWTNLGSYDDNTGSIMINTVATQFITRGMKVP AE
VNNLSGSTSGSCSDIYKKTIGFFKSQKANIQKAYYGTK EESDNWYSKHPNV
KPKGTKISDFCKGREGGTEGTYKHACSMYYYRLVDEDNLVIPFRKLKIPGIP
25 GPKIDECRRKASSKTGCKVADALYKCLKAINGKSFENALKKLDEESSRTY

PRM-P3-A6 (SEQ ID NO:21)

MIRILFPLFILSLGIYQVTCLMCHSCTLDGELESCEDSINETYVVKIEEKECKP
AQSCGKVSFTANGTVRIGRG CIRSSSSWKIDCRILAKEVRDEGIAVTHCSLCD
30 TDLCNE

PRM-P3-F11 (SEQ ID NO:23)

MLQIKHFLFFVVLFFVVAHSNDYCEPKLCKFNNQVKTHIGCKNDGKFVESTC
PKPND AQMIDMTEQRKNLFLKIHNRRLRDLARGSVSNFKSAAKMPMLKWD
NELARLAEYNVRTCKFAHDQCRSTKACPYAGQNLGQMLSSPDFLDPNYVIK
NITREWFLEYKWANQGHTDKYMTGSGKNGKAIGHFTAFIHEKSDKVGCAY
AKLTNQQYNMKQYLVACNYCYTNMLKEGIYTTGKPCSQCQGKKCDSVYK
NLCDASEKVDPIPDIFKQSRQQRSRK

PRM-P5-D6 (SEQ ID NO:25)

10 MIVKSFLGVFLVILLVSVTEQDRGVDGHRRTQDDHDYSELAEYDDDEDPHQE
VIDGDEEEHELSSGRRLSHEDEDDDDRHYGHRGEDRENSRGRNGGSRNRGS
EEQSYDPYSHERAPTYSESSEYDHSGDYDNSNYQQHSSTPSSYSNIDHYLHLI
QLHSVPSDLAQYADSYLQHSKNSIRYYASHAKDFEKIRPCLESVVKYSNLLN
DDLAKEYIRCORKCYLERLNSYTSAISQYTVTTNACINNRLH

PRM-P5-E9 (SEQ ID NO:27)

MIIKLCAIAVACLLTGDGEAAPRATRFIPFAVISDLDKKSIKSDQKSFTSIVRY
 GELKDNGERYTLSEIKSENHLYFTRYAYNGRGAELSELLYFNKLYTIDDKTG
 IIFEVKHGGDLIPWVILSNGDGNQKNGFKAEWATVKGDKLIVGSTGIPWFEE
 20 KTQSLNTYSLWVKEISKEGEVTNINWKSQYSKVKNAMGIPSSVGFVWHEAV
 NWSPRKNLWVFMPRKCTTEYFTSQVEEKTGCNQIITANEDFTQVKAIRIDGP
 VQDQAAGFSSFKFIPGTQNNDFALKTIERNQGQTATYGTVINIEGKTLLNEKR
 ILDDKYEGVAFFKNPEGII

25 PRM-P5-F12 (SEQ ID NO:29)

MHFKIIFCSLFIVLLGHMAFAESESSESSSESSSETSEESSEEVVPSPSPSPKHRP
HFGPHHPHGGRPKPPHPPPKPEPEPDNGSDGGNQDNSNGQDNSNGNSQND
EODNSOSGSAKRFRPAVNIVNLVIPFSTI

30 PRM-P5-F2 (SEQ ID NO:31)

MFSKIFSLAILALALSTVSSETCSNPQVGASSYTTTDTATIVSQIAFITEFSLEC
SNPGAEEKVSLFAEVDGRITPVAVIGDTKYQVSWNEEVKKARSGDYNVRLY

-30-

DEEGYGAVRKAQRSGEENNAKPLATVVVRHSGSYTGPWFNSEILASGLIAV
VAYFAFATR SKILS

PRM-P5-G11 (SEQ ID NO:33)

5 MSNLLTIFGAICFLGVANS LQFPRNP DQTRWAEKTCLKESWAPPN LINKWK
QLEFPSTNLTYCYVKCFVMYLG VYNETTKKFNV DGIRSQFTSQGLRPPNGLE
SLQKTSKGTCKDVFRMSAGLIK KYKLEFVKAFHGDSAEAAK WYIEHKGNV
KAKYQKASEFCKTQKDECRLHCRFY YRLVDEDFQIFNRKFKIYGISDSQLR
QCRSKASQAKGCKVAKVLKNCLDKIDSEKVKTALKTLDEISANYV

10

PRM-P5-H4 (SEQ ID NO:35)

MYFTHTLNFLLLVILLIMAGFSQANPEKRPCTNCERP KLSAKTPL

PRS-P1-B11 (SEQ ID NO:37)

15 MTWVILCVALLVASVVAEGGIDAEGNRTKIEKITAGAGSDGKV VYTEGGSF
PEKLEKEQKSVKKELGELPKPTNATFSP PVKVENKTEEVRNATLPVNATTEA
PKVVNTTASTTTVKLTSTSTTTTPKPKKPSLTISVEDDPSLLEVPVKVQHPQ
TGGRLDVEEPVAQLSHENILEMPVNHRDYIVPIVVLFAIPMILGLATVVIRRF
RDYRLTRHYRRMDYLVDGMYNE

20

PRS-P1-B4 (SEQ ID NO:39)

MKKILLFSVIFVALLITAEAPGKRARP KAPAVTKGRDVPKPRPGQGQVPV
EPDFPMENLRSRI

25 PRS-P1-E7 (SEQ ID NO:41)

MAVKNLHKFLLVVG FVSLIHAAYSAAQHRTYLRITEQEFNSLPFDIVLQAVV
SLIILVYSILQVVG EFREIRAAVDLQAKSWETLGNIPSFYMFNHRGKSLSGQY
EDNIDTSAD

30 PRS-P1-G9 (SEQ ID NO:43)

MMSRWSKSVKFVCLLLCGGFTFLTTSARAKPTLTFQLPPALTNLPPFVGISRF
VERKMQNEQMKYTGVRQTNESLVM IYHDLTIAIVELGPEKSLLGCELEI

-31-

NNDDEGAKVLKELATVNIPLEIDFREMVKLMKQCEKIDYIRKVKRQGAPES
DQTTNRQHQTGYFTGATAGLSILSGILPGTKWCGTGDIARTYHDLGTEATM
DMCCRTHDLCVPKVRSYQQRYNLTKSIYTKSHCKCDDMLFNCLKRTNTS
ASQFMGTIYFNVVQVPCVLDTDGRGYRFRKARTFS

5

PRS-P2-C8 (SEQ ID NO:45)

MKLLPIILLALTVLIVTCQAEHPGKCRREFAIEEECINHCEYKHFGFTDDQF
RIKKHHRENFKNAMSHYGAIKRDQEGELDKLLNRCAKKAKESPATSKRDK
CYRIINYRCVVVDNNLINYSVYVKAVTKINDSINV

10

PRS-P2-G8 (SEQ ID NO:47)

MKELVVFLTLIVLVVICHAEERPSQKCRRELKTEEECILHCEYKHRYFTDDQF
RLNADQRGDFRNIMRRYGAIKRDQESQL
DKHLKKCANKVAKTPATSRKDKCRKISRYHCAVDNKLKFKYNDYANAIK

15 YDKTINV

P. perniciosus polypeptides include polypeptides having a sequence as set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, and conservative variants thereof.

20

Specific, non-limiting examples of an amino acid sequence of a *P.*

perniciosus polypeptide are set forth below:

PERL-P7-G8 (SEQ ID NO:49)

25 MKIFLCLIAVVFLQGVVGFHVEREYAWKNISYEGVDPALFNIDNIPTGFVHD
AINKKIFIAVPRRSPQIPFTLTEDTTKHPERSPPLSKFPGSDKLINVYQPVIDE
CRRLWIADVGRVDYKGDEQKYPNQNAVLIAYDLTKENYPEIHRYEIPSKIAG
SNTIPFGGFAVDVTNPKEGCGKTFVYITNFEDNTLIVYDQEKKDSWKISHGS
FKPEHDSSTLSHDGKQYKYRVGLFGITLGDREDPEGNRPAYYIAGSSTKLFEIST
30 KILKEKGAKFDPVNLGNRGPHTEAVALVYDPKTKVIFFAESDSRQVSCWNT
QKPLNHNKNTDVIFASAKFIYGSDISVDSQLWFLSTGHPPIPNLKLTDFDKPHI
RLMRVDTAKAIRRTRCEVKPRKP

-32-

PERL-P6-H9 (SEQ ID NO:51)

MKIFLCLIAVVS LQGV LAYDI EREYAWKNISFEGIDPASYSVKNSIVTGFAHD
ADSKKIFITIPRLNPVPITLTELDTTKHPEGSPPLSKFPGSDKLISVYQPVIDE CR
5 RLWIVDAGQVEYKGDEQKIPKKNAAILAYDLTKDNYPEIDRYEIPNNVAGNP
LGFGGFAVDVTNPKEGCGKTFVYITNFEDNTLIVYDQEKKDSWKISHDSFKP
EHESILTHNGAQHILKLGIFGITLGDLDEEGNRQAYYLGGSSTKLFRVNTKDL
KKKAGQIEFTPLGDRGSHSEALALAYDPKTKVIFIEYNSKRISCWNTQKSLN
PDNIDVIYHSPDFIFGTDISMDSESKLWFFSNGHPPPIENVQLTFDKPHFRLISM
10 DTKKSIHG TKCEVKP

PERL-P7-C2 (SEQ ID NO:53)

MFKKFILVALVVVVAQCALPAIPIARQGKDFPVPFVSEDNNPDDYFDDQYYP
DINDAGVGSKAPQGSRKPPNRGTIPPRGDQVSSGGRTPPGRVGGTSPTKD
15 KRARPQINRNPTGTVGQGGSPGTKDKRARPQINRNPTGSGTKPRDREL VIRD
KPPSGSQGGKPGRQVRGPKEDLSRYQNAPAKLIFKSSNINTAGKTPKRCEVV

PERL-P6-H1 (SEQ ID NO:55)

MTYFKISTCCLVLISLILPICIK VIRFDDRDEYLLGKPDNTDEELLYSTFDFIK
20 NTCANPKMKCTNNATHFVLDFSDPKKRCISSIHVFSTPDGPVNLEENKPRS
KSSIYCQVGIGQSYCLLVFKKKERREDALVDIRGLKTC SLKERYTSGDPKK
TDAYGMAYKFDKNDNWSIKREGVKQWKRSGNEIFYRKNGLMNHQIRYLS
KFDKYTVTREM VVKHRAKKFTMDFSNYGQYRISFLDVYWFQESVKHKPKL
PYIYYNGECLPSNKT CQLVFDAD EPITYAFVKVFSNPDHNEPRLRHADLGRG
25

PERL-P3-E11 (SEQ ID NO:57)

MKLLITIGAVCVLQVVTVSSIFFPIPINIQTGTTSSSSGQPGQQTTSISFSNVS
NITDMVIYLTQNISRALLTRVPNPDDIKSAADILESFTGSLKYFQTPDDVDQ
EESETKSRSKRSFTDIFKQSSPLKEIGERJEEIKKKLKGMLKPKPQTPSGNQTD
30 SSNTTSETQSRKKRALTD FIPMDSLKDAISK TGEVLIPSSASANS SPLDFMSKL
SDIANDLIQNSMKEISENLASSVAMYQVNSQLDAIKQSM DIKQEIDKTQKIQ
KYVKEALNQAKNATKSLGEK LKSSNCFAQFINPFKLFEKGITCVKNKIDNGL

-33-

KIAKDTFKNLQQAMSVPSDIQSEVSKCSQNQQLNPIAKLLCYLRTPQLDDE
KLLLPFEFTRRIREITNYFATMRMDLIRCGIETIQSIGDKVEDCAREAILAVKD
TLKG

5 PERL-P7-G12 (SEQ ID NO:59)

MKQLVVFLALIVLIVICHAEPSSKKCRSGLVKDEECILHCEYKYYGFTDDNF
ELDSDLRGHFRTAMRKHGAIRIDQERQLDKHLKKCAQEAKKSEKCRKIIQY
YRCAVNNKLFQYNAYAKAIIALDKTINV

10 PERL-P3-C9 (SEQ ID NO:61)

MINSTVIQFIFLVIFLPGKSKSAPKTCEINLPTSIPTKGESIYLLNGNGSVFRPD
GKLTQLNIGDSLISYCPGQKELKRVPCSPKFSLENTCNSNVHSELVDTEEC
GKDGGKCYNISFPLPTNTFHTIYRTCFNKQKLTPIYSYHVIINGKAVGYHVKQP
RGNFRPGKGVYRKININELYKTHISRFKRIIGSTQTFFRKPLHYLARGHLSPEV

15 DFVFGNEQHATEFYINTAPQYQSINQGNWLRVEKHVRKLAKALQDDLHV
TGILGILKFSNKRAEREIYLGEVGPVPQIFWKAVFHPKTSSAIVFVSSNNPHE
KTFNPMCKDVCETARFGGKQHENQNFNHTVGFTICCELPDFLGNSKVILPK
EFQGKNYRKLLKMPGKP

20 PERM-P2-A10 (SEQ ID NO:63)

MNNLLTFFGVLCFLGFANSLRFPDPQTRWAEKTCLREFSRAPPSLLKKW
QQLDFPNTNLTHCFIKCFTSYLGVYNDTTKKFNVDGIKTQFKSQEIPAPQGLE
TLRKTSGTCKDIYLMTVDLVKKKNKLQFAKAFHGISAEEAAKWYTQHKGNV
KGKYQKASEFCKSKDDECRLHCRFYYYRLVDEDYQIFNRNLKINGISNAQL

25 QQCRNKASQAKGCQVAKVLRQCLKDINPENVKATLKELDEISAK

PERL-P6-H11 (SEQ ID NO:65)

MLQIKHFLFFVVLLVIVHANDYCQPKLCTNGKTVKPHIGCRNNGDFDRSAC
PNDAQMVEMTQQRKELFLKIHNRRLDRFARGSVPNFKSAAKMPMLKWDN

30 ELAKLAEYNVRTCKFAHDQCRATTACPYAGQNLGQMLSSPDYLDPGYAIK
NITREWFLEYKWADQQRNTFTGGPGKDGGKQIGHFTAFVHEKSDKVGCAY
AKLTNRQFNMKQYLIACNYCYTNMMNEKITAQVPPF

-34-

PERS-P1-H11 (SEQ ID NO:67)

MIVKGLLGVLVILLVCVTEQGV DGYHRANGDYGYSYENRHHVVNGDEEE
HEIKHTNSRKFD DDDYLFSHGYAAYDDEDEDERQGYSRGGGGAGDSSRD
5 PGFYRRGSQE QSYDPHSGQTAPGYSESSEYEHS GDYDNSQNQQYSSTPSNA
NVNLIDQYLHLIQLHSIPSDLVQYAESYLTHAKNSIRYYAVHAKDFERIRPCL
ESVTKYFNMLNDDLAREYVRCQRQCYLDRLNSYTTAISQYTVTTNACINNR
LN

10 PERM-P2-G11 (SEQ ID NO:69)

MILKLCAIAVLFFLIGDGEAAPRPTRFIPFAISDLHRKAMHDEKNRFTSIVKY
GQLKYNGEKYTLSIRSENLYFTKDTYKGTGADMSELIYFNDKLYTLNDET
GTIYEVKHGGELIPWITLKNDDGNQKDGFKAKWATVKGNKLIVGSAGMAF
LDAKTMNIDRDALWVKEISESGHVTNKYWDSQYKKVRDAMGLVSGFVWH
15 EAVNWSRPNLWVFMPRKCTNEPYTVRLDKKTGCNQIITANENFNDVRAIH
INRAAADPASGFSSFKFIPNTRNNDIFAIKTIERNGQTATYGTVIDINGKTLLP
DQRILDDKYEGIAFFKDPKGIK

PERM-P5-E2 (SEQ ID NO:71)

20 MNTLLKVAVLLSLGGTGYSWQYPRNADQTLWAWRSCQKEHIGDDQALLK
KWLKFEIPDDKVTHCFIKCTWIHLGMYDEKTKTIRVDKVKQQFEGRKLPVP
AEISKLEGPTDGDCEKIYRKTKAFLDAQMKNYRIAFYGIYDGSDAWFAEHP
ETKPKKTKISEFCKGREGGKEGTCKHACSMYYYRLVDEDNLVIPFRKLPGIS
ESDLKQCRDAASKKSGCQVADDNLRLS

25

PERM-P5-C11 (SEQ ID NO:73)

MKYFSLNLLIVILLIVACSPQLPCLPQDSKKKPSNRPKLSARSGLSY

PERM-P5-H8 (also referred to as P2-G9) (SEQ ID NO:75)

30 MKKIVLFSFIFVALVISAKAIETELDDPDDATKGRDVAKAEPGQLGQVPVVP
DLNPSNTRKRRNRSRKRRRN LGKRLKKVFA

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PERL-P3-B3 (SEQ ID NO:77)

MMSRWSKSVKFVCLLLCGGFTFLTTSARAKPTLTFQLPPALTNLPPFIGISRF
VERKMQNDQMKTYYTGVRQTNDLSLVMYHHDLTIAIVELGPEKTLGCELIEI
NNDDEGAKVLTELATVNIPLQIDFREMVKLMKQCEKIDYMRKVKRQGASE
5 SDQTTNRQHQGTGYFGLGGATAGLSILSGILPGTKWCGTGDI AKTYHDLGTE
ATMDMCCRTHDLCVPKVRSYQQRYNLSNNSIYTKSPCKCDDMLFNCLKRT
NTSASQFMGTIYFNVVQVPCVLDTERGYRFRKARTFS

PERM-P2-D11 (SEQ ID NO:79)

10 MKQLVVFLALIVLIVICHAKRPSRKCRSGMVKEEECILHCEYKYYGFTDDKF
QLDADQQRGNFRFAMMDYGAIRMDQEGQMDEHLKKCANEA EKAPVCSKV
DKCRKIIQYYRCAVNNKLFQYNAYAKAIALDKTINV

PERM-P5-E3 (SEQ ID NO:81)

15 MKQLPVILLALVFLIAKCRSEKPEYKCRRDFKTEDKNCFLSCTFKNYHFIDN
KFRIERKNIENYKKFITDYKALKPNVSDNDLEKHLDCWDKFQKSPEASTRP
EKCEKVNNFERCVIDKNIFDYPIYFNALKKINYITKV

PERM-P2-F11 (SEQ ID NO:83)

20 MKKIVLFSVIFIALVISAKAIEDEDDDDDDDESED RDVARAEREQQEEEPDEP
EYIPSRPRNRSKMRKWRNRNYRKYRDESRKRKRDMVLDVIRFL

Homologous polypeptides having an amino acid sequence at least 75%, 80%,
25 85%, 90%, 95%, 98%, or 99% identical to the amino acid sequence as set forth as
SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ
ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ
ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ
ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ
30 ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47, SEQ ID NO:49, SEQ
ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ
ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ

ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83 are disclosed herein.

Fragments, variants, and fusions of the *Phlebotomus* polypeptides identified above are disclosed herein and can readily be prepared by one of skill in the art using molecular techniques. In one embodiment, a fragment of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide includes at least 8, 10, 15, or 20 consecutive amino acids of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide. In another embodiment, a fragment of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide includes a specific antigenic epitope found on a full-length *P. ariasi* polypeptide or on a full-length *P. perniciosus* polypeptide.

In one embodiment, a fragment is at least 17 amino acids, at least 23 amino acids, at least 25 amino acids, or at least 30 amino acids in length from any polypeptide (including polypeptides as given in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, conservative variants thereof, and homologues thereof), or any fragment that retains at least an epitope.

One skilled in the art, given the disclosure herein, can purify a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide using standard techniques for protein purification. The substantially pure polypeptide will yield a single major band on a non-reducing polyacrylamide gel. The purity of the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide can also be determined by amino-terminal amino acid sequence analysis.

Minor modifications of the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide primary amino acid sequences may result in peptides which have substantially equivalent activity as compared to the unmodified counterpart

polypeptide described herein. Such modifications may be deliberate, as by site-directed mutagenesis, or may be spontaneous. All of the polypeptides produced by these modifications are included herein.

Polynucleotides encoding salivary polypeptides from sand fly species of the subgenera of *Phlebotomus* Larroussius, in particular *P. ariasi* and *P. perniciosus*, are disclosed herein. Also provided are nucleic acid sequences encoding a *P. ariasi* or a *P. perniciosus* polypeptide. Specific, non-limiting examples of *P. ariasi* nucleic acid sequences include SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48, and degenerate variants thereof. Specific, non-limiting examples of *P. perniciosus* nucleic acid sequences include SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84, and degenerate variants thereof. These polynucleotides include DNA, cDNA, and RNA sequences that encode a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide. It is understood that all polynucleotides encoding a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide are also included herein, as long as they encode a polypeptide with the recognized activity, such as the binding to an antibody that recognizes the polypeptide, the induction of an immune response to the polypeptide, an effect on survival of *Leishmania* when administered to a subject having leishmaniasis, or who undergoes a decrease in a sign or a symptom of *Leishmania* infection.

The polynucleotides of the disclosure include sequences that are degenerate as a result of the genetic code. There are 20 natural amino acids, most of which are specified by more than one codon. Therefore, all degenerate nucleotide sequences are included in the disclosure as long as the amino acid sequence of the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide encoded by the nucleotide sequence is functionally unchanged.

Specific, non-limiting examples of a polynucleotide encoding a *P. ariasi* polypeptide are set forth below:

PRL-P4-A10 (SEQ ID NO:2)

```
      ACTTGTCGATCACTTTTCACTCGCTCCAGACGCATTTTGTGCGTCT
5  TCAGCCGTGATTAGCACAAAGTGTTTTAGAATTTGGTGAAAAAATAGCA
   AGATAAGGATGAAATTAGTGCCATTGTGTATTTTAGTGTGTTTTCTAATC
   ATCGCGCAGCAGGTGGCTCAGAATGAAGCATCTCCCGCCAAAAGCCAAG
   ACGCCATGTACGGTGATTGGAGTCGTTGGAGCTCCTGTGACGAGACTTG
   CCATCAGACGAAGGTGAGATCGTGCCTAGGGGCTGTCTGTGAGCGGAAT
10  CGACTGATGAAGGAGCGAAAATGTCCAGGATGTGGTACAAAAGTGCGA
   ATGTACAGAACTTCTTCAGCTCTTCGGCATGGGAGACTCCATAGAGAC
   TGA CTATGAAGATGACTATGGAGAGCACTGGCTAACTGATGACAGAGTC
   ATTAGTTCTAGGAATGATCCTGAAAGTGCAGAAAGTGATGAATTGGGAT
   CATTCTTCAGGGATTTCTTCCATTCA TTCGATTTTGAGTGGA AAAATCCA
15  TTTAGCAATCCCATGAGAACAATGATGTGGACTTGGAGGTGGAGGAAG
   ATGAGGAAGTTGAAGAACTTCCCGAAATTAGGACTTCTAATGAGGAGGA
   TTCTGTCTCTGGGGCGGATCACGTGTGTGGAGTGACCAAGAATGAGAGA
   TCTTCAGGGATGATGGCAAAA ACTATCGGCGGGAGGAACTCGAAGAAG
   GGTCGATGGCCCTGGCAAGTGGCTCTTTATAACCAGGAATATGAGAATT
20  TCTTCTGCGGCGGGACTCTTATCTCAA AATACTGGGTCATAACGGCCGCT
   CACTGTCTGATATCTGACTTCGGCAGTGACATCACGATCTTCTCCGGCCT
   GTACGACACCGGAGATCTCGTGGAGTCGCCCTACAGCATCCACCTGGTG
   CGGGATCGAGTGATTCATCCGCGCTACGACGCCGAAACCAATGACAATG
   ATATCGCCCTGCTGAGGCTCTACAACGAAGTGAAATTGAGCGATGATGT
25  GGGTATCGCTTGTCTGCCCAGCTACTCGCAAGCCTCCCCGGGACGCAGTG
   AGGTGTGCAAGGTGCTGGGCTGGGGCCAAGGGACACGTCGAACCAA ACT
   CCAGGAGGCCGACATGCACATCCAACCCGCCAACTCCTGCAAGCGCCAC
   TACTACGGCACCGGACAACTCGTCACGCGTCACATGCTGTGCGCCTCCTC
   CCGGA ACTACGTCAGCGACACGTGTGGCGGTGATTCCGGTGGACCACTG
30  CTGTGTCGCGACACCAAATCCCCCGCCCGACCCTGGACGCTGTTCCGGCAT
   CACGAGCTTCGGTGACGATTGCACGGTGAGCGAGAGTCCGGGTGTTTAT
   GCGCGCGTCGCCTCCTTCCGGAAGTGGATTGACTCCGTCATCGAGTGCGA
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CGGCTCTTGTGACAATTAATAAACTCACAATATTATCAGTGAAAAAATA
AATTAGCAAATTTAATGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRL-P4-A9 (SEQ ID NO:4)

5 AAAATGAATATCTTATTGAAAGTTGCGATTTTGGTGAGCTTGTGC
GAAATTGGGTACTCTTGGAATATCCCAGGAATGCCGATCAAACCTCTCT
GGGCTTGGAGATCATGCCAAAAGGGAACTATGACCCAGAATTAGTGAA
GAAATGGATGGCTTTTGAAATCCCAGACGACGAAGTAACTCATTGTTAC
ATTAAGTGTGTTTGGACTCATTGGAATGTACGATGAACTAGCCAAA
10 CTATTAGAGCTGATAGAGTCAAGCAACAATTCAAGGCTCGTGGACTATC
AGTTCCTGCTGAAATAAGCCATTTAGAGGGATCTACAGGAGGATCCTGT
GTAACGATTTACAAAAAACTAGGGCTTTCCTTGAACTCAAATGCCGA
ATTATCGCATTGCATTCTATGGCACTGTGGAAGAATCAGATAAGTGGTTC
GCCGAATAATCCCGAACTAAACCCAAGAGAATTAAGATTTCTGACTTCT
15 GCAAAGGTCGCGAAGCTGGAACGGAAGGAAGCTTGCAAGCATGCTTGCA
GCATGTACTACTACCGCTTAGTCGATGAGGATAATCTTGTGATTCCCTTC
AGGAAGTTGCCAGGAATCTTAGATTCCCAACTTGAACAATGCAGGGATC
AAGCTAGTTCGGAACTGGATGCAAAGTTGGTGATACAATCTACAATTG
TCTTAACAGAATTAATCCGGAAGGTCTTAAAAAAGCATTGAATACACTC
20 GATGAACAATCATTGACGTTGTATTAGAAAGCAATAAACTTGATTAAGA
AAAACAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRL-P4-C10 (SEQ ID NO:6)

GTCAGTCTTTTGGAAACAAAACATGAAGATCTTCTGTGCCTTTTT
25 GCTGCAGTTTCCATTCAGGGAGCTTTAGCTTCTCAAATTGAAAGGGAATA
CGCGTGGA AAAACATTATTTATGAAGGGATAGATCAAGGATCCTACAAC
ATTGAAAACAGCATCCCAACTGCTTTCGCTCACGATGCAGCTAGTAAGA
AGATTTTCATCACTATTCCAAGAATAAACCAAGTACCAATAACCCTAACT
GAATTTGATAGCATCAAGTATCCGGGAGGTTCTCCTCCTCTTAGCAAATT
30 CCCTGGAAGCGATAACATAATTTCCGTTTATCAACCGGTCATTGACGAAT
GTCGTAGACTTTGGATTGTGGACGCTGGACAGGTTGAGTACAAGGGAGA
TGAGCAGAAGTATCCCAAGAAAAATCCTGCTATCATAGCTTATGACCTG

-40-

ACTAAGGACAATTATCCTGAGATTGATCGATACGAGATACCGATTAATA
TTGCTGGTAATCCATTAGGATTTGGAGGATTTACCGTTGATGTTACCAAT
CCGAAGGAGGGATGTGGTAAAACCTTTTATCTACATCACAACTTCGAAG
ACAACACTCTGATTGTGTACGATCAGGAGAAGAAAGATTCTTGGAAGAT
5 CAGTCATGGTTCATTTAAACCCGAACATGAGTCGATTCTAATCCATAACG
GGGTTGATCATATTTTAAAACCTGGGTATTTTCGGAATCACCCCTTGGAGAT
CGGGATTCGGAGGGAAACCGTCCGGCTTACTACTTAGGAGGAAGCAGTA
CGAAGCTCTTTGAAGTCAACACAAAGGCTCTTAAGAAGAAGGAGGGTGA
AATCGAACCAATCACTCTGGGAGATCGTGGACCTCATTCCGAAGCCATT
10 GCTTTGGCATAACGATCCCAAGACCAAAGTGATTTTCTTCACTGAATATAA
CTCTAAGAAGATCTCATGCTGGAACATCAAGAAACCCCTTATTCATGAC
AACATGGATAAGATTTATGCTAGTCCTGAATTTATTTTCGGCACTGATAT
TTCGGTTGATAGTGAATCCAAATTGTGGTTCTTCTCCAACGGACATCCAC
CCATTGAGAATCTGCAGTTGAGCTCTGATAAGCCTCATATTCATCTTATA
15 AGCGTGGATACGGAAAAGGCAATTCGTGGCACTAAATGTGAAGTGAAG
GCCTAAGTCAAAAATATAACAATTTTACAACAAATTGTAAATTTAACGA
TGATAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRL-P4-D6 (SEQ ID NO:8)

20 GTCTTTTGGAAACAAAGATGAAGATCTTTATGGGCCTAATTGCT
GTGGTTTCCCTTCAGGGAGCTTTAGCTTATCACGTTGAAAGGGAGTACGC
GTGGAAGAACATTACTTTTGAAGGGATAGATCAAGCATCCTACAACATT
GAAAACAGCATCCCAACTGCATTCGTTACGATGCACTTAGTAAGAAGA
TTATCATCGCTATTCCTAGGCTATATCCTCAGGTGCCAATTACTTTAACTC
25 AACTTGATACCAACCAAGCATCCGGAACGTTCTCCTCCTCTCGAAAAATTC
CCTGGAAGCGATAAATTAACCTCTGTTTATCAACCGATGCTTGACGAATG
TCGTAGACTTTGGATTGTTGACGTTGGACAGGTCGAGTACAAGGGAGAT
GAGCAGAAGTACCCCAAGAAAAATCCTGCTATCATAGCCTATGACCTGA
CTAAGGACAATTATCCAGAGATTGATCGATATGAGATACCGATTAATAT
30 TGCTGGTAATCAAATAGGATTTGGAGGATTTACCGTTGATGTTACGAATC
CGAAGGAGGGATGTGGTAAAACCTTTATCTACATCACGAACTTCGAAGA
CAACACTCTGATTGTGTACGATCAGGAGAAGAAAGATTCTTGGAAGATC

-41-

AGTCATGGTTCATTTAAACCCGAACATGAGTCTAATTTCTCCCACAACGG
TGCTCAGTACAAGTACAAAGCGGGTATTTTCGGAATCACCTTGGAGAT
CGGGATCCGGAGGGAAATCGTCCGGCTTACTACTTAGGAGGAAGCAGTA
CGAAGCTCTTTGAAGTGAGCACTGAGGCTCTCAAGAAGAAGGGTGCAAA
5 GTTCGATCCTGTTCGTCTGGGTGATCGTGGGCGTCACACTGAAGCCATTG
CTCTGGTATATGATCCCAAGACTAAAGTTATTTTCTTTGCTGAATCTGAC
TCGAGACAAATCTCATGCTGGAACACCCAGAAGCCACTAAATCATAAGA
ATACTGATGTAATTTATGCGAGTTCCAAATTTATTTTCGGCACCGACATT
CAAATTGACAGTGACTCCCAATTGTGGTTCTTATCCAACGGACAACCCCC
10 CATTGATAATCTCAAATTGACTTTTGATAAGCCCCATATTCGTCTTATGA
GGGTAGATACGAAAAATTCAATTCGTAGGACTAGATGTGAAGTGAAGCC
CATCAAGAAGCCATAAGACAATCTATTA AAAAATGTAACAATTTCCCCAA
AAAAAGAAATTGTAAATTTTACGATGATAATAAAAAAATTTTATGCTTGT
GAAAAAAAAAAAAAAAAAAAAA

15

PRL-P4-D7(SEQ ID NO:10)

ATTCAGTCATAAACCTGGGGTAATGTTTAAGGAAATTATCGTAGT
GGCTCTAGCCGTGATCGTGGCACAATGTGCTCCTCCTGCAATTCCAATTG
CAAAACAGGGAAACGATTTCCCTGTCCCAATTGTTGATGAAAAGGAAAC
20 GGATGATTTCTTTGACGATCGATTCTATCCGGACATAGATGATGAGCGTG
TAGGTGCTAGGGCTCCGGTGGGTGGCAAACAGACATCTAATAGAGGAAC
CAGTTCTCAGAGTGATAAGGTTCTCGTCCTCAAGGGTCCAATAGAGGG
CCTAGCTCTCAGACTACTGACAAGGTTCCCCGTCCTCAATGGCCCAGTAG
AGGAACCAATTCTCAGAATGACAAGGTTCTCGTCCTCAAGGGTCTAGT
25 GGACAAACTCCACCTAGAACGCCTGGAAAGGTTGAACAAAGTGGAAGG
ACCAACACAAAGGACCAAATACCTCGTCCACTGACTAACAGAAACCCAA
CCAAGAACCAACTGAACAGGCTAGAAGACCAGGAAACAGGGAGCTAC
TCATTAGGGATAAAACCCAGGGAGTCAAGGTGGAAAACAGGGAAACAG
GCAATAGGCAGAACTGTCGAGTTATAAAGACGCTCAGCCGAAGTTGAT
30 TTTCAAATCGAGTCAATTCAATACTGATGGCCAAAATCCATATTTAACGA
GGTTGTTCAAGACGAAGAAAGTCGAAGAAGTTATAGCTAAAGGAAGTCC
CACTGATGAATATGTCCTGGAGCTTTTGGATGGAAAGCCAGATAATCTG

-42-

AGCTTGGTCATCAGAACAAATGGCAAGACGAGCCAAGCGGTTCTCAGGA
ATCCCACTCGCAACAGAATTGTGGGCCGTATCAAGTCGTACAACCCCGG
CCCGAGGCGAATGTCCTATTAATTTTTTTTTTCTCTTTTTTCTCCTAAATAC
AACTCCCACAATAAAATTTTCAGTTGTACGCAGCAAAAAAAAAAAAAAAAAA
5 AAAAAAAAAAAAAA

PRL-P4-E5 (SEQ ID NO:12)

TAACGCTCAAGCTTTGTCTTCAATATGGCTTCCATCAAGCTCAGTA
CTTGCTCTTTGCTTTTGCTAAACCTCATTCTACCAACAATCTCTATGAAAG
10 TTATCAGTTTCGACGATAGAGATGAGTATCTACTTGGTAAACCTGCAAAT
TCTGACGATGAACTTCTCTATTCAACCTTTGACTTCCAGAGAGATCCCTG
TTCTAAGTCTTACGTGAAGTGCACCAACAACAACACCCACTTTATTCTGG
ATTTGCTTGATCCGAAGAAGAGATGCATCTCTTCAATTCACGTTTTCTCC
TACCCCGATAGACCTCCCAGCTTTGAGGAGAAGAGGATTCCCTCGAAGA
15 GTGCAATTTACTGCCAAAAGGGCGGCATTGGGAAGAGTCACTGTTTGCT
GGTGTTTCAGGAAGAAGGAACCTCGAGAGGACGCACTGGTTGATATCCGG
GGAATCCCCGCTGATCAAACATGCTCCCTCAAGGAGCGCTACACATCGG
GAGATCCTAAGAAAACCGATGCTTACGGAATGGCCTATCAGTTTGATAG
AAAAGATGATTGGCACATTCAAAGAACAGGTATCAAGACATGGAAAAG
20 ATCAGGAAACGAGATCTTCTACCGTAAGAATGGTTTAATGAACCATCAA
ATAAGGTACTTGAGCAAGTTCGACAAATACACGGTTACCAGAGAATTGG
TGGTGAAGAACAACGCTAAGAAATTCACCTTGGAATTTTCAAACCTCCGT
CAATACCGAATCAGTTTCTTGGACATCTACTGGTTCCAGGAGTCTCAGAG
GAATAAACCCAGATTACCTTATATTTACTACAACGGTCATTGCTTGCCTA
25 GCAACAAGACATGCCAGTTGGTCTTCGACACTGATGAGCCTATTACTTAT
GCTTTTGTGAAAGTGTTTAGTAATCCGGATCACAATGAACCACGACTAA
GACATGAAGATCTAGGACGAGGGTAAGAATGGACTAGTCCGGGGTTGA
AAAATCGCCTAAAATATGGGGAATCTATTATTGAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAA

30

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PRL-P4-F3 (SEQ ID NO:14)

ATGTATCAAACATCACGGATATGGTGATTTATCTCACGCAGAATA
TCAGTAGAGCTCTTCTCACGCTTCTACCAAATCCTGAAGATGTCCGATCA
GCAGCGGATGTCCTAGAAAGTTTTACAGACGACCTCAAGTCTTTCTACCC
5 ACCTCCTGATGATGTGAATGAAGAGGTATCAGAGACAGAGTCAAGAACT
AAGAGATCATTGATTGAGCAACTCAAAGAGTCGCAACCTCTAAAACAAA
TCAGAGAAACAGTTGCTGAGACAACCAAGTACCTAAAGGGATTCTTAAA
AACGAAACCTTCTGGAAATCAAACGGAGAGTTCTAACTCAACAAGTACG
AAGACTCAGTCAAGAAAGAGACGTGGATTAAGTATTTATACCAGTGA
10 ATTCTCTAAAGGATGCAATTTACAAAGCAACTTCAGGTGCCATGAAAGC
GTTCAAACCTTCAAGTGAAAATAAAACAAGTTCAAATCCTCTAGATTTCC
TCGCAAGCCTCTCAGATATTTCCAGAGATCTTGTACAAAATTCAATTAAG
GAAGTCTCTGGCAATTTAGTTTCAAGCGTTGCTTTATACCAAGTCAACTC
AAAGTTAGATGCCATTAAACAATCCATTGGTATCATAAATCAAGAAATT
15 GATAGGACCAAAAAAGTTCAGCAATACGTCATGAATGCTCTTCAACAAG
CCAGCAATATTACTAACTCAATTGGAGAGCAACTCAAGTCCAACAACCTG
TTTCGCACAATTTATAAACCCATTCAAACCTTTTCGAAGAAGTAATAACTT
GTGTGAAAAATAAAATCGAAAATGGATTGAAAATTGCGGAAGAGACATT
TAAAAATTTAAATCAGGCTTTAAGTGTGCCCTCAGATATTGTAAGTGAAG
20 TGTCCAAATGTTCCCAAACCAGAACTTGAATCCCTTGACGAACTTCTG
TGCTACTTGAGGGTACCCCTGCAATTGGATGAGGAGAACTGCTGCTTCC
TATTGAATTTGCGAGGCGAATTAGAGAAATAACCAACTATTTTGCCACC
ATGAGAATGGACCTCATTCAATGTGGCATAGCAACTATTCAATCAATCG
GAGACAAGGTTGAGAATTGTGCAATAGAAGCAATATTGGCTGTAAAGGA
25 CACTTTGAAGGGATAAAGTCCGTATTTTATGCTGTCCAATTGGGCTAACC
CAATCATTGATATACCGAATTGTGTATGTATATTGAGAAAATGAATAAAT
GCTTCAAATGAAAAAAAAAAAAAAAAAAAAA

PRL-P4-G12 (SEQ ID NO:16)

30 ACATACGATTCCTAACCAACCATGAAGCAGTTCCCAGTGATCCTT
TTGACCTTAGGCCTTTTGGTCGTGAAATGCCGATCAGAACGGCCGGAAT
GGAAATGTGAAAGAGACTTCAAGAAAATCGACCAAAATTGCTTTCGTCC

-44-

- TTGTACATTTGCAATTTACCACTTTGTTGATAACAAGTTCAGGATTGCCA
GGAAGAATATTGAAAACACTACAAGAAGTTCTTAATTGACTATAACACCGT
GAAGCCCGAAGTTAATGATTTGGAAAAACACCTGTTAGATTGTTGGAAT
ACAATCAAATCCATTGAAGCATCATCCAGGACGGAAAAATGTGAACAAG
5 TTAACAACCTTTGAACGATGTGTTATTGACAAGAACATTCTTAATTATCCT
GTTTACTTCAATGCTTTGAAGAAAATAAATAAGAATACAAATGTTTAATT
AAATAAAGATGTGAAATATTGCAGTGCACAAATATAAAAAAAAAAAAAA
AAA
- 10 PRL-P4-G7 (SEQ ID NO:18)
AGAAGTTATTTTACACCTGTGCAATGATAAACCCAATAGTGCTGA
GATTTACTTTTCTCTTGGTGATTTTGTTCCTGGCAAATGTAAAAGTGCCC
CAAAGTCTTGCACCATTAATCTTCCCACCAGCATTCCCAAGAAAGGTGA
ACCGATTTACCTCAACAGTAATGGATCAGTTTTCGACCTATTGGAGGTT
15 TAACTCAACTCAACATTGGGGACTCCCTCTCCATCTACTGTCCACCACTG
AAGAAGCTCAAGAGTGTTCCCTTGCAGTCGAAAATTCTCCCTTGAGAGCT
ACTCTTGCAACAACAGCTCTCAGAGTGAACCTCGTGCAGACGGAGGAGGA
GTGCGGACAAGAGGGGAAATGGTACAACATTGGCTTTCCATTGCCACA
AATGCCTTCCACACAATCTACAGAACTTGCTTCAATAAGCAGAACTAA
20 CACCAATTTACTCTTATCACGTCATCAATGGAAAGGCCGTTGGATATCAC
GTGAAGCAGCCGCGAGGAACTTCCGACCAGGAAAAGGTGTCTACAGG
AAAATCAACATCAATGAGCTGTACAAGACGCACATTTTCGCGCTTCAAGA
AAGTCTTCGGTGACAAACAGACATTCTTCCGGAAGCCACTGCACTACCT
GGCTCGCGGACATCTCTCCCCTGAAGTGGACTTTGTCTTCGGCACCGAAC
25 AACACGCCACTGAGTTCTACATCAACACCGCCCCCAGTATCAGTCCATC
AACCAGGGAAATTGGCTGCGAGTTGAAAAACACGTGCGCGGTCTGGCCA
AGGCGCTCCAGGACAATCTCCTCGTCGTCCTGACATTTTGGACATCCTA
AAGTTCTCAAACAAACGAGCCGACACAGAAATCTACTTGGGCGACGGAA
TAATTCCTGTTCCGCAAATATTCTGGAAGGCAATCTTCCACCTCAGAACA
30 TCTTCCGCCATTGTCTTTGTACCTCCAACAACCCTCACGAGACGACCTT
CAACAATATCTGCAAGGACGCGTGTGAAATGGCAGGATTTCGGAGACAAA
CAACATGGAAATCAAAATTTTCCAACCTACTCCTTGGGATTACCATCTG

-45-

TTGCGAACTACAGGACTTCATTGGGAACTCGAAAGTTGTTCTTCCAAAGG
ATATTCAAGTCAAAAACCAACCGCAAACCTTCTTCAGTTGCCAAAACCGAA
GCAATAAACTTTAATTTTGGTCTTGCAAAGTGTGAGTATATTTTAAATAA
ACAGCAAATCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

5

PRL-P6-E11(SEQ ID NO:20)

AGTCTCTCCCAGGGTTTTATTGTGGAAAATGAACGCTTTATTGCTT
TGTGTTTTGTTGAGTTTAAGTGGAATAGGGTACTCTTGGAATACCCTAG
GAATGCCGATCAAACCTCTCTGGGCTTACAGAACGTGCCAAAGAGAAGGG
10 AAAGATCCGGCATTAGTATCCAAGTGGATGAATTGGGTGTTACCAGATG
ATCCGGAAACTCACTGCTACGTTAAGTGCCTTTGGACCAATTTAGGATCC
TACGATGATAACACCGGTTCCATTATGATTAACACAGTGGCTACACAATT
TATAACACGCGGCATGAAAGTCCCAGCCGAAGTAAATAATTTAAGTGGG
TCGACAAGTGGATCTTGTTTCAGATATTTACAAGAAAACCATTTGGGTTCTT
15 CAAAAGTCAAAAGGCGAACATACAGAAAGCGTATTACGGAACCTAAGGA
AGAGTCAGATAACTGGTATTCGAAACATCCAAATGTAAAGCCGAAAGGA
ACGAAGATTTCTGACTTCTGCAAAGGTCGCGAAGGTGGAACGGAAGGAA
CTTACAAGCATGCTTGCAGCATGTACTACTACCGCTTAGTCGATGAGGAT
AATCTTGTGATTCCGTTTCAGGAAGTTGAAAATTCCGGGAATTCCAGGACC
20 CAAAATAGATGAGTGTAGGAGGAAGGCTAGCTCGAAAACCTGGATGCAA
AGTTGCCGATGCACTATACAAATGTCTTAAGGCTATAAACGGTAAAAGT
TTTGAAAATGCTTTAAAGAAGTTGGACGAAGAATCATCCAGAACTTATT
AAAATAAAAGAACTTGAGTTGCTAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAA

25

PRM-P3-A6 (SEQ ID NO:22)

ATATCTAGAGGAAAATATTAAGTGAAAAGTGAAATGATTAGGATT
CTGTTTCCTCTCTTTATTCTTAGTCTTGGAATTTATCAAGTAACTTGCCTT
ATGTGCCACTCATGTACTCTTGATGGGGAGCTTGAGTCATGTGAAGATTC
30 TATCAATGAGACTTATGTAGTTAAGATTGAGGAAAAGGAGTGCAAACCT
GCGCAATCTTGCGGAAAAGTCTCATTTACTGCGAATGGAACAGTTTCGAA
TCGGAAGAGGATGTATTCGCTCAAGCAGTAGTTGGAAAATCGATTGCAG

-46-

AATACTTGCAAAGGAAGTTAGAGATGAAGGCATTGCGGTAACACACTGT
TCCTTATGCGACACGGACTTGTGCAATGAATAAATAAAATTGTGAAGAA
AAAAGTATTGTAAGTGTACTGGAAAAACAATTTTCAGAAATATCCACAA
TAAAAAGAGAGCATTTCGCTGTAAAAAAAAAAAAAAAAAAAAAAAAAAAA
5 AAAA

PRM-P3-F11 (SEQ ID NO:24)

TCCAGTTAATATTCCGACATGTTGCAAATTAAACACTTCTTGTTCT
TTGTGGTGTGTTCTGTTGCTCGCTCACTCCAATGATTATTGTGAGCCGAAA
10 TTGTGCAAATTTAACAACCAAGTGAAGACTCACATTGGATGCAAGAATG
ATGGAAAGTTCGTGGAAAGCACTTGCCCAAACCAAATGATGCTCAAAT
GATTGATATGACTGAACAGAGGAAGAATCTCTTTCTCAAGATTACAAT
CGCCTTCGCGATAGGCTCGCTCGTGGTTCTGTGTCTAATTTCAAGTCAGC
CGCCAAGATGCCAATGCTGAAATGGGACAATGAATTGGCCAGGTTGGCA
15 GAATACAATGTGAGAACGTGCAAATTTGCTCACGATCAGTGTGCTCAA
CCAAGGCTTGTCTTATGCTGGCCAGAACTTGGGCCAAATGTTGTCTTCT
CCAGATTTCTTGGACCCCACTATGTCATCAAGAATATCACTAGGGAGTG
GTTCTTGGAGTATAAGTGGGCAAATCAAGGACATACTGATAAATATATG
ACAGGATCTGGTAAGAATGGCAAAGCAATTGGTCACTTTACTGCCTTCAT
20 CCATGAGAAAAGCGACAAGGTTGGATGCGCTGTTGCTAAATTAACCAAC
CAGCAGTACAACATGAAGCAGTACCTCGTGGCCTGCAACTACTGCTACA
CGAATATGCTAAAGGAAGGGATCTACACGACAGGAAAGCCTTGTTCTCA
GTGCCAGGGAAAGAAGTGTGATTCCGTCTACAAGAACTTATGCGATGCG
AGTGAGAAAGTCGATCCCATCCCAGACATCTTTAAGCAATCGAGACAAC
25 AGAGGAGCAGGAAATAATTCTCTGCTTTCCCATTTGGTATAAAATGTTAA
ATTTATTGTTTTCCCATCTATTGGGTGAATTGGCGAAAAAGGTGAAGATG
AAAAAAGGTATAAGAAAATAAGAGATAAACAGAACTGAGATATCTGA
AA
AAAACCCAA

30

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PRM-P5-D6 (SEQ ID NO:26)

TCAGTTTCACTTTGACCATCGATGGTGCAATTACTTCAATTCAATT
TACGAAATCACTTTGATTGAGAAACGATGATCGTGAAGAGTTTCCTTGG
GGTGTTTCTTGTGATCTTGCTCGTGTCCGTGACAGAACAGGATCGTGGAG
5 TAGACGGACACAGGAGGACTCAAGATGACCATGATTACAGCGAATTGGC
GGAATATGACGACGAAGATCCTCATCAAGAGGTAATTGACGGTGATGAG
GAGGAACATGAGTTGTCCGGAGGACGTCGACTATCCACGAAGACGAAG
ACGACGACGACAGACACTATGGCCATCGTGGAGAGGATCGAGAGAATTC
TCGAGGCAGAAATGGTGGATCTCGTAATCGTGGTAGTGAGGAACAATCA
10 TACGATCCCTACAGCCACGAGAGAGCTCCTACCTACTCAGAATCCAGTG
AATACGACCACAGCGGTGACTACGACAATTCCAACACCAGCAACATTC
CTCCACTCCCTCCTCCTACAGCAACATCGATCACTATCTCCATCTCATCC
AATTGCACAGCGTCCCCAGTGATTTAGCCCAGTACGCCGATTTCCTACCTT
CAACACTCCAAGAACTCCATCAGATACTACGCTTCGCATGCCAAAGACT
15 TTGAGAAGATTGACCCCTGTCTGGAGAGCGTCGTGAAGTACTCCAATCTC
CTCAATGACGATCTTGCCAAGGAGTACATCAGATGCCAACGAAAGTGTT
ACCTTGAACGTCTCAATAGCTACACATCGGCTATCTCTCAGTACACAGTC
ACCACAAATGCCTGCATAAACAACCGATTGCATTAAAGCTGAGGATTAT
CTTGTGAAATATTTATTTGAATCGATCAGTGAAAATAAATTTCCAATAGC
20 AAAAAAAAAAAAAACAAAAAAAAAAAAAAAAA

PRM-P5-E9 (SEQ ID NO:28)

AAAGTATTCAGTTGTGAGAAATCTTTCCAAATACACATCATGATT
ATCAAATTGTGCGCTATTGCTGTTGCTTGTCTCCTCACTGGAGATGGAGA
25 AGCAGCTCCCAGAGCAACAAGATTCATCCCTTTGCTGTTATCTCCGACT
TGGACAAGAAGTCCATTAAATCCGATCAGAAGAGTTTCACCAGCATCGT
GAGATATGGCGAATTGAAGGACAATGGAGAGAGATATACGTTATCCATC
AAGAGTGAAAATCTTCACTACTTCACGCGATACGCTTACAATGGACGCG
GAGCCGAATTATCTGAATTGTTGTACTTCAACAACAACTCTACACCATT
30 GATGACAAAACAGGAATTATCTTTGAGGTGAAACATGGTGGGGATCTCA
TTCCATGGGTGATCCTGTCGAATGGCGATGGAAATCAAAGAATGGCTT
TAAAGCCGAATGGGCGACAGTTAAGGGTGACAAGTTGATTGTTCGGATCA

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ACAGGAATCCCCTGGTTTGAGGAGAAAACCCAGTCTCTTAACACCTACA
GCCTTTGGGTGAAAGAGATCAGCAAGGAAGGCGAAGTCACCAACATCA
ATTGGAAGAGTCAATACAGCAAAGTGAAGAATGCAATGGGAATTCCTTC
CTCTGTGGGATTTCGTCTGGCATGAGGCTGTAAATTGGTCACCGAGGAAG
5 AATCTATGGGTCTTCATGCCCAGAAAATGTACAACCTGAATATTTACCAG
TCAAGTGGAAGAGAGAAAACCTGGATGCAATCAGATTATCACGGCTAATGAA
GATTTCACTCAAGTGAAAGCAATTAGGATCGATGGACCTGTTTCAGGATC
AAGCTGCTGGATTCTCCTCCTTTAAGTTCATCCCAGGCACTCAAAACAAT
GATATCTTCGCACTGAAGACTATCGAGAGGAACGGCCAAACAGCCACTT
10 ACGGGACAGTAATTAACATCGAAGGGAAGACTTTGTTGAACGAAAAACG
AATTCTCGATGATAAATACGAAGGAGTTGCATTTTTCAAGAATCCCGAA
GGCATTATATAAAATAATAATGATGGAGTGAAAAACAAATTGAAATAAA
ATGCTAAAGCTCATAAAATTAATAAAAAAAAAAAAAAAAAAAAAAAAAA
AAA

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PRM-P5-F12 (SEQ ID NO:30)

ATCAATTGTTATTGAAATAATCTTCAAGATGCATTTCAAGATTATC
TTCTGCTCCCTCTTCATTGTCCTGCTGGGACATATGGCGTTTGCTGAATCT
TCTGAGTCATCATCTTCAGAGTCGTCGTCTTCAGAAACATCTGAAGAGTC
20 ATCTGAAGAAGTTGTTCCATCCCCCTTCTCCCTCACCTAAGCATCGGCCGC
ATTTTGGTCCCCATCACCCACATGGAGGCCGACCTAAGCCTCCCCATCCG
CCGCCACCGAAACCTGAGCCGGAGCCAGATAATGGCTCAGATGGTGGCA
ATCAGGATAATTCAAATGGTCAGGATAACTCTAATGGAACTCTCAGAA
TGATGAACAGGATAACTCTCAATCGGGATCCGCTAAGCGATTACAGACAA
25 CCTGCAGTGAATATTGTTAATCTTGTGATTCCTTTTTCTACGATTAACTT
TCCTTTTGTCTACTTTAATCACTTTAATGCACGTAATAATAAAAAATACTT
TCAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRM-P5-F2 (SEQ ID NO:32)

30 TTTCTCAATTTGTGTGTGATTGCTCTAGACGTGGCCGGTGAATTTT
CCCAAAATGTTTTCCAAAATCTTCTCTTTGGCTATCCTCGCTCTCGCCTTG
TCCACTGTGTCCAGTGAGACTTGCAAGTAATCCTCAAGTGAAGGGCGCTTC

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CTCCTACACAACCACGGATGCAACGATAGTCAGCCAAATTGCCTTCATC
ACTGAATTCTCACTGGAGTGCTCGAATCCCGGAGCTGAGAAGGTCTCCCT
GTTGCGCCGAAGTTGACGGACGGATCACTCCAGTTGCGGTAATTGGAGAT
ACTAAATATCAGGTGAGCTGGAATGAGGAGGTCAAGAAGGCTCGCAGTG
5 GAGATTACAATGTAAGACTGTACGACGAGGAGGGATACGGAGCTGTGCG
CAAAGCCCAGAGATCAGGAGAGGAGAACAATGCGAAGCCACTGGCTAC
AGTTGTTGTTGCGCCATTCCGGATCCTACACTGGCCCTTGGTTCAATTCTG
AAATCTTAGCCTCCGGTCTCATCGCCGTCGTAGCATATTTTGCTTTCGCC
ACCAGAAGCAAAATCCTGTCGTAGAGACGCATCAATAATTCACAAAAA
10 TGTAGCCAGAAGGCTGTTCTTGGCACTCAGACTGTTTCTGTGAAATACAA
CAACATATCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRM-P5-G11 (SEQ ID NO:34)

GTTTCTTATACATCACTTTGAAGCAGCAATGAGTAACTTGCTAACT
15 ATCTTTGGGGCAATTTGTTTCTTGGGCGTTGCCAACTCTCTGCAATTCCT
CGGAACCCAGACCAAACCAGATGGGCAGAAAAGACATGTTTAAAGAA
TCTTGGGCACCACCTAATCTGATAACAAGTGGAAGCAATTGGAATTC
CCAGTACCAATCTCACCTACTGCTACGTGAAGTGCTTTGTTATGTATTTA
GGAGTCTACAACGAGACGACCAAGAAATTCAACGTAGACGGTATCAGAT
20 CCCAATTTACAAGTCAAGGACTTCGTCCACCTAACGGTCTAGAGAGCCT
ACAAAAGACATCTAAAGGAACCTGCAAGGATGTCTTCCGAATGTCCGCT
GGCCTAATCAAGAAGTACAAATTGGAATTCGTAAAAGCTTTCCATGGAG
ATTCTGCCGAAGCTGCGAAGTGGTACATCGAACATAAAGGAAATGTAA
GGCAAAGTATCAGAAAGCTTCGGAATTCTGCAAAACTCAGAAGGATGAG
25 TGTAGGCTGCATTGTCGTTTCTACTACTACCGCTTAGTTGACGAAGACTT
CCAAATATTCAATAGAAAATTCAAGATCTACGGCATTTCGGACTCACAG
CTACGGCAGTGTAGGAGTAAAGCCAGTCAAGCTAAGGGTTGCAAGGTTG
CCAAAGTCCTTAAAAATTGCCTCGACAAGATTGATTCTGAGAAAGTGAA
AACCGCTCTTAAGACTTTGGATGAGATATCAGCAAATTACGTTTAAACAGT
30 AATCTCCAAGTTAGCCCCATCAGCCTAATTTAGCGCCACCTTTAAATCAA
CCCCCAGCTAATTTCTCGAACGTTAGAAAAAGGTGTTTAACTTACGGGTG

-50-

ATTGAGTGTAAGTAATTTAGCGGCTGTGGAGATGAAATGACTATTAAAT
CGTGCACAATGGGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PRM-P5-H4 (SEQ ID NO:36)

5 ACAATTCATATTTCTTTAGTGAAGTTGTTGAAAATCAAGCAAGA
TGTACTTTACCCATACCCTCAATTTTCTTCTTCTTGTAATTCTATTAATAA
TGGCTGGTTTTTCCCAGGCAAATCCCGAGAAAAGGCCCTGCACAACTG
TGAGCGTCCCAAGTTATCGGCTAAAACCTCTTTGTAACCCTTTTAAATCA
TATAATCGGTGATTAAAGATTTACCAGCAGAGCTACCGCAATGTGAAAT
10 CGAAAAATTATACCTACCTACAGAAAAACTAAAATGTAATAAGAATTAG
AAAAAATAAAAATGATCCAAGAACAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAA

PRS-P1-B11 (SEQ ID NO:38)

15 ATCGCGATTCTGTTGCAACGTCACAGAGTACTTCCTTCTTTTCCTT
TCGGTTTCCTATCATTTCAATTTGTTATCTCGCACCCAAATGACGTGGGTG
ATTCTTTGTGTCGCCCTCCTGGTTGCTTCCGTTGTGCGGAGGGCGGAAT
CGATGCGGAGGGGAATCGCACGAAAATCGAGAAGATAACCGCGGGTGC
AGGAAGTGATGGCAAGGTGGTCTACACAGAGGGTGGAAGCTTCCCGGA
20 GAAGCTAGAGAAGGAGCAGAAGAGCGTGAAGAAGGAGCTTGGAGAATT
GCCAAAGCCCACAAATGCCACATTTTCACCTCCCGTGAAGGTGGAGAAT
AAGACGGAGGAGGTGAGGAATGCTACACTGCCGGTGAATGCCACAAC
GAGGCCCTAAGGTGGTCAATACGACAGCCAGCACCACCACGGTGAAGC
TAACATCCACCAGCACCACAACAACCTACTCCCAAGCCCAAGAAGCCCAG
25 CCTCACGATTAGCGTGGAGGACGATCCGAGCCTCCTGGAGGTGCCAGTC
AAGGTGCAGCATCCACAGACCGGAGGACGACTGGATGTGGAGGAGCCT
GTGGCTCAGCTGTCGCATGAGAACATCCTGGAGATGCCCGTGAATCACC
GGGACTACATTGTTCCCATTTGTGGTGCTTATCTTTGCCATTCCCATGATCC
TGGGACTCGCCACTGTTGTCATCCGACGTTTCAGGGACTACCGGCTCACT
30 CGCCACTACCGCCGGATGGACTACCTCGTGGATGGAATGTATAATGAGT
AGTTTCCGGCTCGCACTAACCGCCCAAGCAATAATCTAATTAATGCTTAA

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TCGTTTTATACTATGTAAATAAATGTACATTTTAATAATAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAA

PRS-P1-B4 (SEQ ID NO:40)

5 CGTCAGTTTGTGAAAGTTGGGAAAATGAAGAAAATTCTGCTATT
CAGTGTTATATTCGTTGCTTTGTTGATCACTGCCGAAGCCATTCCGGGAA
AACGGGCAAGACCGAAAGCTCCCGCGGTCACTAAAGGTCGGGATGTTCC
AAAACCAAGACCTGGTCAAGGAGGACAAGTGCCAGTTGAACCAGATTTT
CCTATGGAAAACCTTAAGAAGTAGAATTTAGTAGATCTTCAGCTTTCTCGG
10 CCCCTTTAATAAAAATTCGTCTACTGATAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAA

PRS-P1-E7 (SEQ ID NO:42)

ATATATCTATCGATTTCTCGTGTTTTGATTTGCTTAGGTGGCCCCA
15 TTTTCCAAGAAAATTCCTGAAATGGCAGTTAAAAATCTTCACAAATTCC
TCCTGGTTCGTGGGATTTCGTGTCCCTGATCCATGCGGCTTATTCGGCAGCA
CAGCACAGAACGTACCTGAGAATCACGGAGCAGGAGTTTAATTCTCTCC
CATTTGACATTGTGCTCCAAGCTGTGGTGAGTCTGATCATTCTGGTGTAC
AGCATTCTGCAGGTTGTTGGGGAGTTCCGGGAGATTTCGAGCAGCTGTGG
20 ACTTGCAAGCGAAATCATGGGAGACTTTGGGTAACATCCCCTCCTTCTAC
ATGTTCAATCACCGTGGGAAGAGCCTATCCGGCCAGTATGAGGATAACA
TTGACACGAGTGCCGATTGAATGCCCGGAAGAAGCCTTCCCGTAAATCT
ATTTGAATGTAAGGAATCCGATTAATTGAATTAACACCAAAGGAGAGCT
GAGGGAA
25

PRS-P1-G9 (SEQ ID NO:44)

CACGAATTAGAAAACGGTCCAGTGATTCTCTCGGTGGCTGATTT
ATAAGAGAATGTGAAGAGTTGAGGATGATGTCTCGCTGGAGCAAAAGTG
TGAAATTTGTGTGCCTCCTCCTGTGTGGCGGATTCACGTTTCTCACAACA
30 TCAGCACGTGCCAAACCCACACTGACCTTTCAGCTACCGCCCGCACTCAC
GAACCTACCCCCCTTCGTGGGCATCTCACGATTCGTCGAACGCAAAATGC
AGAATGAGCAGATGAAGACCTACACTGGCGTTTCGGCAGACGAATGAGTC

-52-

TCTCGTGATGATCTACCACCATGATCTGACGATCGCCATCGTGGAATTGG
GACCAGAGAAGAGTCTCTTGGGTTGTGAATTGATAGAAATTAACAACGA
TGACGAAGGCGCCAAAGTGCTGAAAGAACTGGCCACGGTGAATATACCA
CTGGAGATCGACTTCCGGGAGATGGTGAAGCTCATGAAGCAGTGCGAGA
5 AGATCGATTACATACGGAAAGTGAAACGCCAAGGAGCACCAGAGAGTG
ACCAGACGACAAATCGTCAACACCAGACGGGCTACTTCACGGGCGCCAC
TGCCGGCCTGAGTATCCTCAGTGGCATCCTTCCCGGCACCAAGTGGTGTG
GCACAGGAGACATCGCCAGGACATATCACGATCTCGGCACAGAGGCTAC
CATGGACATGTGCTGTGCGACTCACGATCTCTGTCCAGTGAAAGTGCGCT
10 CATATCAGCAACGCTACAATCTCACCATAAGTCAATCTACACAAAATC
TCACTGTAAATGTGATGACATGCTGTTCAATTGCCTCAAGAGGACCAAC
ACGTCAGCCTCGCAATTCATGGGGACCATCTACTTCAACGTGGTCCAAGT
GCCATGTGTTCTGGACACAGACAGAGGCTACAGATTCAGAAAAGCGAGA
ACCTTCTCCTGATCATCGCAATGCAACGAAATCTGAGGATATTTTATTTT
15 TGGGGACTTTTTTTTTCGCTGTAAAGACCATTCTGTGATTTTCAGCTGAG
GTGCTCTTTCAAATGAATTATTTATATGTTACAAAAAAAAAAAAAAAAAAAA
AAAAA

PRS-P2-C8 (SEQ ID NO:46)

20 AACATATCTGAACCAGCCATGAAGTTGTTACCTATAATTCTGTTG
GCGTTGACAGTCTTGATCGTGACTTGTCAAGCTGAACATCCCGGTACTAA
GTGTAGAAGAGAATTCGCAATAGAAGAAGAATGTATCAATCATTGTGAA
TACAAACACTTTGGCTTCACAGATGACCAATTCCGGATTAAAAAGCATC
ATAGAGAAAATTTCAAAAACGCTATGAGTCATTACGGTGCAATCAGAAA
25 GGATCAAGAAGGTGAACTGGATAAGCTTTTGAATAGATGTGCCAAGAAA
GCCAAAGAGTCTCCTGCTACATCGAAAAGAGACAAATGTTACAGAATTA
TTAACTACTACCGTTGTGTTGTTGTAGATAATAATCTGATCAATTATTCTG
TTTACGTCAAAGCTGTTACCAAGATTAATGATTCAATCAATGTATAAAAA
TCAAATATTACTTTGAAATAAAAGAAGAAACAATGTTGTATGCAAGGCC
30 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

Specific, non-limiting examples of a polynucleotide encoding a *P*.

PERL-P7-G8 (SEQ ID NO:50)

TATATATAACTTTTGAAATGTTCAAGTCAGTCTTTTGGAAAGCAAAGATGAA
GATCTTTCTGTGCCTAATTGCTGTGGTTCCTTCAGGGAGTTGTAGGCTT
TCACGTTGAACGAGAATATGCGTGGAAAAACATTAGTTACGAAGGAGTA
20 GATCCAGCATTATTCAATATTGATAATATCATTCCGACTGGTTTCGTTCA
CGATGCAATTAATAAGAAGATTTTCATTGCTGTTCCAAGGAGATCTCCTC
AAATACCATTTACCCTAACTGAACTTGATACCACCAAGCATCCGGAACG
TTCTCCTCCTCTAAGCAAATTTCTGCTAGCGATAAATTAATCAACGTTT
ATCAACCGGTCATTGACGAATGTCGCCGACTTTGGATTGCGGACGTCGG
25 ACGGGTTGACTACAAGGGGGATGAGCAGAAGTATCCAAACCAAAATGCT
GTTCTCATAGCTTATGACCTGACGAAGGAAAATTACCCAGAGATTCATC
GATACGAGATACCAAGTAAAATTGCTGGTTCAAATACAATTCCATTTGG
AGGATTTGCCGTTGATGTTACGAATCCGAAGGAGGGATGCGGCAAAACC
TTTGTCTACATCACGAACTTCGAAGACAACACTCTGATTGTGTACGATCA
30 GGAGAAGAAAGATTCTTGGAAGATCAGTCATGGGTCATTCAAACCAGAG
CATGACTCGACTCTCTCCCATGACGGTAAACAGTACAAGTATAGAGTGG
GTTTATTTCGGAATTACTCTTGAGATCGGGATCCGGAAGGAAATCGTCC

-54-

GGCTTACTACATAGCCGGAAGCAGTACGAAGCTCTTTGAGATCAGCACT
AAGATTTTGAAGGAGAAGGGTGCCAAATTTGATCCTGTTAATTTGGGAA
ATCGTGGTCCCCACACTGAAGCTGTTGCCCTGGTATATGATCCCAAGACA
AAAGTTATCTTCTTTGCTGAATCTGACTCCAGGCAGGTCTCTTGCTGGAA
5 TACCCAGAAGCCACTGAATCATAAGAACACTGATGTGATTTTTGCCAGT
GCCAAATTTATTTACGGCTCCGATATTTCAAGTTGATAGTGAATCTCAATT
GTGGTTCTTATCCACGGGACATCCACCCATTCTAATCTCAAGTTGACCT
TTGATAAACCCCATATTCGTCTTATGAGGGTGGATACGGCTAAAGCAATT
CGTAGAACTAGATGCGAAGTGAAGCCCCGCAAGCCATAAGACGAATATC
10 TAATATCAAAAATGTTACAATTCTGCTAAAATGTCTAAAAATAAAGATA
ATAATAAATAAATAAAAATATTGTGCAACACACAGAAACAAACCAAAA
AAAAAAA

PERL-P6-H9 (SEQ ID NO:52)

15 CAAGATGAAAATCTTTCTGTGCCTAATTGCTGTGGTTTCCCTTCAGGGAG
TTTGTAGCTTATGATATTGAGAGGGAATACGCGTGGA AAAACATCAGTTTT
GAAGGAATAGACCCAGCATCCTACAGCGTTAAAAATAGTATCGTAACTG
GTTTCGCTCACGATGCAGATAGTAAGAAGATTTTCATTACTATTCCAAGG
CTAAACCCAGTTCCGATTACTCTAACTGAACTGGATACCACTAAGCATCC
20 GGAAGGATCTCCTCCACTAAGCAAATTTCTGGTAGTGATAAATTAATCT
CTGTTTATCAACCGGTCATTGACGAATGTCGCCGACTTTGGATTGTGGAC
GCTGGACAGGTTGAGTACAAAGGAGATGAGCAGAAGATTCCCAAGAAA
AATGCTGCTATTATAGCTTATGATCTGACGAAGGACAATTATCCAGAAAT
TGATCGATACGAGATACCGAATAATGTTGCTGGTAATCCACTTGGATTG
25 GAGGATTTGCCGTTGATGTTACAAATCCGAAAGAGGGATGTGGTAAAC
CTTTGTCTACATCACGAACTTCGAAGACAACACTCTAATAGTGTATGATC
AGGAGAAGAAAGATTCTGGAAGATCAGTCATGATTCAATCAAACCTGA
GCATGAATCGATCCTGACCCACAACGGTGCTCAACACATTTTAAAGTTG
GGTATATTCCGAATCACCTTAGGAGATCTGGATGAGGAGGGAAATCGTC
30 AGGCTTACTACTTGGGAGGTAGTAGTACGAAGCTCTTTAGAGTGAACAC
CAAGGATCTCAAGAAGAAAGCCGGTCAAATTGAATCACTCCTCTGGGA
GATCGTGGATCTCACTCTGAAGCCCTTGCTCTGGCTTATGATCCCAAGAC

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TAAAGTTATCTTTTTTCATTGAATATAATTCTAAGCGAATCTCCTGCTGGA
ACACTCAGAAATCACTAAATCCTGACAACATTGATGTGATTTATCACAGT
CCTGATTTTATCTTCGGCACTGATATTTCAATGGATAGTGAATCCAAAT
TGTGGTTCCTTTTCCAACGGTCATCCACCAATTGAGAATGTTCAACTAACT
5 TTTGATAAGCCACATTTTCGTCTTATAAGCATGGATACGAAAAAATCAAT
TCATGGTACTAAATGCGAAGTAAAACCTTAAGTCAAACCTTGAAAAATAA
AACACTTCTTAAAGAAATTGTAATTTTTATGATGGTAATAAATTTTTGTG
TGCCGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

10 PERL-P7-C2 (SEQ ID NO:54)
CACTTTAGTCTCAAATCTTGGATCATGTTTAAGAAATTTATCTTGGTGGC
CCTTGTCGTTGTCGTGGCACAATGTGCTCTTCCCGCAATCCCAATTGCAA
GACAGGGAAAAGATTTCCCGTCCCGTTTGTAAGTGAAGATAATAATCC
GGATGATTATTTTGACGATCAGTACTATCCGGACATAAACGATGCGGGT
15 GTAGGTCAAAGGCTCCGCAGGGAAGCAGAAAGCCACCCAATAGAGGC
ACCATCCCTCCTCCTCGTGGTGACCAAGTGTCATCTGGTGGACGAACTCC
ACCCGGAAGGGTTGGACAGGGTACAAGCCCTACAAAGGATAAAAGAGC
TCGTCCTCAGATTAACAGAAACCCAACCGGAACGGTTGGACAGGGTGA
AGCCCTGGTACAAAGGATAAAAGAGCTCGTCCTCAGATTAACAGAAACC
20 CAACCGGAAGTGGTACAAAACCCAGAGATAGGGAGCTTGTGATTAGGG
ATAAGCCCCCATCCGGAAGTCAAGGTGGTAAACCTGGAAGACAGGTCAG
AGGCCCAAAGGAAGATTTGTCGCGTTATCAAAACGCTCCGGCAAAGTTG
ATTTTCAAATCGAGTAATATCAATACTGCTGGTAAAACCCCGAAGCGCT
GTGAAGTTGTTTAAGACGAAGAAGGACAAAACAGTTGTTGCTAAGGGAG
25 GTCCCAACGATGTTTATGAGGTGGAGCTTCTCGATGGAAATTTCAATAAT
ATGAGCTTGAGGATCCAGATAATGGACAGGAAGAGCAGCACAGCGATC
CTCAGCAATCCAGATCGCAACTTAATTGTTGGCCGTGTCAAGACGTACCG
CGGATTAAGATGAGGTGCTGAATTTTTAAATTTTATTTTATTTTTTTGCTC
CTAAATCCAAAATCCCCCAAATAAATCAGTTTGAACGCAAAAAAAAAA
30 AAAAAAAAAAAAAAAAAAAAAA

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PERL-P6-H1 (SEQ ID NO:56)

GGCCATTACGGCCAGGGGGAATAAGTTAGTGTCTTCACGTTTATTGAAG
CTTTCACCTTCAATATGACTTACTTCAAGATCAGTACTTGTTGTTTAGTTTT
AATAAGCCTCATTCTACCTATAATTTGTATTAAAGTTATTCGTTTTGATGA
5 TAGAGATGAATATCTTCTTGGTAAACCTGATAATACTGATGAAGAACTCC
TCTATTCAACCTTTGACTTCATTAAGAATACCTGCGCTAATCCTAAAATG
AAATGCACCAATAACGCCACTCATTTTCGTTCTGGATTTCTCTGATCCGAA
GAAGAGATGTATCTCCTCCATCCATGTATTTTCCACTCCCGATGGACCTG
TTAATCTTGAGGAGGAGAATAAGCCTCGATCAAAGAGTTCAATTTACTG
10 CCAAGTGGGCGGCATTGGACAGAGTTACTGTTTGCTGGTGTTTAAAAAG
AAGGAACGTCGTGAGGATGCTCTGGTTGATATCCGGGGACTCAAAACAT
GCTCCCTCAAGGAGCGCTACACATCTGGAGATCCCAAGAAAACCGATGC
TTACGGAATGGCATACAAATTCGACAAGAATGATAATTGGAGCATCAAG
AGAGAAGGTGTTAAGCAATGGAAAAGATCAGGAAATGAGATCTTCTACC
15 GCAAGAATGGTTTGATGAACCATCAAATAAGATACTTGAGCAAGTTTGA
TAAGTACACGGTTACCAGAGAAATGGTTCGTGAAGCACCGCGCTAAGAAA
TTCACCATGGACTTCTCCAACATATGGCCAGTACAGAATCAGTTTCTTGGA
CGTCTACTGGTTCCAGGAGTCCGTGAAGCACAAGCCGAAGTTACCCTAC
ATCTACTACAATGGCGAATGCTTGCCTAGCAATAAGACGTGTCAGTTGGT
20 TTTTCGACGCTGATGAGCCTATTACTTATGCTTTTGTGAAAGTGTTCACTA
ATCCGGACCACAACGAACCACGATTGAGGCATGCAGATCTGGGACGAGG
ATAGGAGTGGATTAGTCCGTTGTTGAAATTTGAATAAAATGCTATGAAG
ATGTTAAATTTGCCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

25 PERL-P3-E11 (SEQ ID NO:58)

AAAACATCTTCGCGTTTTTCGTGCTATTTGAAACGGAGAACATCGAGTAA
AGAATATGAAGTTACTAATTACTATCGGTGCGGTTTTGTGTGTTACAAGTC
GTTACAGTATCATCCATCTTCTTTCCCATTCCAATCAACATCCAAACAGG
GACGACATCATCATCATCAGGACAACCAGGACAGCAAGTTACAACGAGT
30 ATAAGTTTCAGTAATGTATCAAACATCACGGATATGGTGATTTATCTCAC
GCAGAATATCAGTAGAGCTCTCCTTACGCGTGTACCAAACCCTGATGAT
ATCAAATCAGCAGCGGATATCTTGGAAGTTTTACAGGAAGCCTCAAGT

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ATTTCCAAACACCTCCGGATGATGTGGATCAAGAGGAATCAGAGACAAA
GTCACGATCTAAGAGATCATTTACTGATATATTCAAACAATCTTCGCCTT
TAAAAGAAATCGGAGAAAGGATCGAAGAAATAAAAAAGAACTAAAAG
GAATGCTCAAACCAAACCGCAAACACCTTCTGGAAATCAAACCTGATAG
5 CTCGAACACAACCTTCGGAGACTCAATCGAGAAAGAAACGGGCTTTAACT
GACTTTATACCAATGGATTCTCTGAAAGATGCGATTTCAAAAACAGGGG
AAGTGTTGATACCTTCAAGTGCAAGTGCAAACCTCTAGTCCTCTAGATTTT
ATGTCAAACCTATCCGATATCGCAAATGATCTTATTCAAACCTCAATGAA
GGAAATCTCCGAAAATTTAGCCTCAAGCGTTGCTATGTACCAAGTCAACT
10 CACAGTTAGATGCCATTAAACAATCCATGGATATTATAAAACAAGAAAT
TGATAAGACCCAAAAGATCCAGAAATACGTAAAGGAAGCTCTTAATCAA
GCCAAAAATGCTACTAAATCTTTAGGAGAAAAGCTTAAGTCCAGTAACT
GTTTCGCTCAATTTATAAATCCCTTTAAACTTTTTGAAAAAGGAATTACT
TGTGTGAAAAATAAAATCGATAATGGATTAAAAATCGCAAAAGACACCT
15 TTAAGAATTTACAACAGGCAATGAGTGTGCCCTCAGATATTCAAAGTGA
AGTGTCCAAATGCTCCCAAAATCAGCAATTGAATCCCATTGCCAAACTCC
TGTGCTACTTGAGGACACCACTGCAATTGGACGACGAGAAGTTGCTGCT
TCCCTTTGAATTTACGAGGAGAATTAGAGAAATAACTAACTATTTTGCCA
CCATGAGAATGGACCTCATTCGTTGTGGCATAGAACTATTCAGTCGATC
20 GGAGACAAGGTTGAGGATTGTGCAAGAGAAGCAATATTGGCTGTAAAG
GACACTCTGAAGGGATAAAGTCCGCATTTTCTGGCTGTCCAATTGGGACT
AACCCAATCATTGATGATGCCGAGCTATTGTATGTTGGAGAAAATGAAT
AAAAGGCTTCGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

25 PERL-P7-G12 (SEQ ID NO:60)
ATTAGAAAACCAATCATGAAGCAGCTTGTTGTATTTTTGGCGTTGATAGT
TCTGATAGTGATTTGTCACGCAGAACCACCTTCGAAGAAGTGTAGGAGT
GGACTGGTGAAAGATGAGGAGTGTATACTCCATTGTGAATACAAATACT
ATGGCTTTACTGATGATAATTTCGAACTTGATTCAGATCTAAGAGGACAC
30 TTTAGAACTGCTATGAGGAAGCACGGCGCAATTAGGATCGATCAGGAAA
GACAACTTGATAAGCATTTGAAAAAATGTGCTCAGGAAGCTAAAAAGTC
GGAAAAGTGTAGGAAAATCATTCACTACTATCGCTGTGCTGTGAATAAT

-58-

AAACTTTTCCAATATAATGCTTATGCTAAAGCAATTATTGCGCTTGATAA
GACAATAAATGTTTAAAAAAGAAAGTGAAATGTATCTATCGCTCAAATA
AAGAAGGAAGCTAAGATCGTTGAAAGAAAAAAAAAAAAAAAAAAAAA
AAAAAAA

5

PERL-P3-C9 (SEQ ID NO:62)

GCTTTAGAAGTTATTTTACATCTGTGCAATGATTAACACAGTGATTC
AATTTATTTTCTTTTGTGATTTTCTTCCTGGAAAATCTAAAAGTGCCC
CAAAGACTTGCGAAATTAATCTTCCCACCAGTATTCCGACAAAAGGTGA
10 ATCAATTTATCTTCTCAATGGAAATGGATCGGTCTTCCGACCGGATGGAA
AATTGACTCAACTCAATATTGGGGATTCCCTGTCCATCTACTGTCCTGGA
CAGAAGGAGCTCAAGAGAGTCCCTTGCAGTCCCAAATTTTCCCTTGAGA
ACATCACTTGCAACAGCAATGTTACAGTGAATTGGTTGACACGGAGGA
AAAGTGCGGAAAAGATGGAAAATGTTACAATATTAGCTTTCCATTGCCA
15 ACAAATACCTTCCATACAATCTACAGAACTTGCTTCAACAAGCAGAAAC
TAACACCAATCTATTCTTATCACGTCATCAATGGAAAGGCAGTTGGATAT
CATGTGAAACAGCCACGAGGAACTTTTCGACCGGGAAAAGGTGTCTACA
GGAAGATCAACATCAATGAGCTCTACAAGACCCACATTTTCGCGCTTCAA
GAGAATCATCGGATCCACCCAGACATTCTTCCGGAAGCCCCTGCACTATC
20 TGGCTCGTGGACATCTCTCACCTGAAGTGGACTTTGTCTTTGGCAACGAA
CAACACGCCACTGAGTTCTACATCAACACCGCCCCCAATATCAATCCAT
CAACCAGGGAAATTGGCTTCGAGTGGAGAAACACGTGCGCAAACCTGGCC
AAGGCCCTCCAGGATGATCTCCACGTTGTCACTGGAATTTTGGGCATCCT
CAAGTTCTCAAACAAACGAGCCGAAAGAGAAATCTATCTGGGCGAAGG
25 AGTTATTCCTGTACCGCAAATATTTTGGAAAGGCTGTCTTCCACCCTAAAA
CCTCTTCCGCCATTGTCTTCGTGTCCTCTAACAACCCTCATGAGAAGACC
TTCAATCCAATGTGCAAGGATGTTTGTGAAACAGCAAGATTCGGAGGCA
AACAACATGAAAATCAAAATTTTCCAATCACACAGTGGGATTCACCAT
CTGTTGTGAATTACCAGACTTTCTTGGAAACTCAAAGTTATTCTTCCTA
30 AGGAGTTTCAAGGCAAAAACCTACCGCAAGTTGCTTAAAATGCCAGGAAA
GCCATAAAAACCTTTCATCTTATGGTGTGTCACACGGCAATAGTTTTGAC
AACAGATCCTAGCTCAAACGGAATTCAATAGCATTTTCCTTTAGAAAAC

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ATCATATTTTCATCGAAAAACAGTCTCTTACAATTCTGAGGATTTTAAA
AAAGAATTTCAATTGAATCAGAATCTCTTTAAGCACTGAAGAGAATCTC
CTGTCATTTTCTGATCTTCTATGGGTCTTTTCCAGAAAATTCTTGATTATT
CCTAAGAAGAAATTGATATTTAGTGAAGACTGTAATTGTTTAGCATTCAA
5 CAGTAAAAATTTGTTGACAGAGCTATAATTCCGTGTGACAACACCATTA
GTGGAAGACTCAACAAATCGATAAAAAAATGATTTCAAAATGGTATAA
TAGTAAAAATAAAAAACCTTTCCGGCAATAAATTATTCCTTTGAGGATCAC
AATGTCCTGAATATTCACACAGTGACTGAGTTTAAAGATTATTTTACTCT
CAAATCGTATAATAAAGGACAAAAACATGCGTAAATAAAGAAATTTGC
10 AGTACGTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PERM-P2-A10 (SEQ ID NO:64)

CCATTACGGCCGAGGAGTCTCTTTCAACGCTTAATATCAGCAATGAATAA
CTTGTTAACATTCTTTGGAGTACTTTGCTTCTTGGGCTTTGCTAACTCTCT
15 GCGATTCCCTCGTGACCCAGACCAAACCAGATGGGCGGAAAAGACTTGT
CTGAGAGAATTTTCTCGTGCTCCACCTAGTCTTTTAAAGAAATGGCAACA
ACTGGACTTTCCAATACCAATCTCACCCACTGCTTCATCAAGTGCTTCA
CTTCGTATCTTGGAGTCTACAACGACACGACTAAGAAATTTAACGTGGA
CGGAATTAAAACCCAATTTAAAAGTCAGGAAATTCCTGCACCTCAAGGT
20 CTTGAGACACTTCGTAAAACATCTAAAGGAACCTGCAAGGATATTTATCT
AATGACTGTGGACCTTGTCAAGAAAAACAAGCTACAATTCGCAAAAGCT
TTCCATGGAATTTCTGCAGAAGCTGCAAAATGGTATACCCAACATAAAG
GAAATGTTAAGGGAAAGTACCAGAAAGCATCGGAATTCTGCAAATCTAA
AGATGATGAGTGTAGGCTCCATTGCCGATTCTACTACTACCGCTTAGTTG
25 ACGAGGACTACCAGATATTCAACAGAAATTTAAAAATCAACGGTATTTT
CAACGCTCAACTTCAGCAATGCAGGAACAAAGCCAGTCAAGCTAAGGGT
TGCCAGGTGGCAAAGGTCCTAAGGCAATGTCTCAAAGACATTAATCCTG
AAAATGTAAAAGCGACTTTGAAGGAGTTGGATGAGATATCGGCGAAATA
ATATACTTAAATTAACCCCATCAGCCCAATTTAGCGTAATTTCTCGACCG
30 TAGAAAAAGGTGTTTAACTTACGGGTGATTGAGTGTAAGTAATTTAGCG
GCTGTGGGAGATGAAATGACTATTAAAAGGTTTATATCCCCAAAAAAAAA
AAAAAAAAAAAAA

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PERL-P6-H11 (SEQ ID NO:66)

AGTAAGTTTATCTGCGCGAGCGGAAATGGGTGCCATTTAGGCCGGAGTC
CAGTTAATATTCCGACATGTTGCAAATTAAACATTTCTTGTTCTTTGTGGT
5 GTTACTCGTGATCGTTCACGCTAACGACTATTGCCAGCCGAAATTGTGCA
CAAATGGCAAAACAGTGAAGCCTCACATTGGATGCAGGAATAATGGAG
ATTTGATAGAAAGTGCCTGTCCAAATGATGCTCAGATGGTTGAAATGACT
CAACAGAGGAAGGAGCTCTTTCTTAAGATTCACAATCGCCTTCGCGATA
GGTTCGCTCGTGGCTCAGTGCCCAATTTCAAGTCAGCCGCCAAGATGCCA
10 ATGCTGAAATGGGACAATGAATTGGCCAAGTTGGCAGAATACAATGTGA
GAACGTGCAAATTTGCTCACGATCAGTGTGCGCAACCACAGCTTGTCCT
TATGCTGGTCAGAACTTGGGGCAAATGTTGTCATCTCCAGATTATTTGGA
CCCCGGCTATGCCATCAAGAATATCACCAGGGAGTGGTTCTTGGAGTAT
AAGTGGGCAGATCAACAACGTACCAACACCTTTACGGGAGGACCTGGTA
15 AAGATGGCAAACAAATTGGTCACTTTACTGCCTTCGTCCATGAGAAGAG
CGACAAGGTTGGATGTGCTGTTGCTAAATTAACGAACCGACAATTCAAC
ATGAAGCAGTACCTCATCGCTTGCAACTACTGCTACACGAATATGATGA
ACGAGAAGATCACAGCACAGGTGCCCCCGTTCTAAGTGCCAGAGTAAAA
AATGCGATTCCAAATACAAGAATTTGTGCGATGCCAGTGAGAAAGTCGA
20 AGCCATCCCAGACATCTTCCTCAAGAAGCGCAGGACATAATTCTCTGCTT
TCCCATTGAAAATTGTAAAATAAATATTGTTTTCCCTTCTATCAGGTGA
ATTGGTGAAGATGAGAAGAAAGAATGTATAAGAAAATAAGAAATAAAC
AGAAACTGAGATATCGTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

25 PERS-P1-H11 (SEQ ID NO:68)

ATCAGTTTCACTTTGACCATCGATGGTGAAATACTTCAATTCATTTTACG
AAATCACTCTGATTGAGAAACGATGATCGTGAAGGGTCTCCTTGGGGTG
TTTCTTGTGATCTTGCTCGTGTGCGTGACAGAACAGGGAGTGGACGGATA
CCACAGGGCTAATGGGGACTATGGTTACAGCTACGAAAACCGGCATCAC
30 GTAGTCAACGGAGATGAGGAGGAACATGAAATAAAACATACTAACTCTC
GTAAATTTGATGATGACGACTATCTCTTTAGTCACGGCTACGCCGCCTAC
GACGACGAAGACGATGAAGATGAACGACAGGGCTATTCAAGGGGCGGT

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GGGGGAGCCGGAGACAGTAGCAGAGATCCCGGATTTTATCGTCGTGGAA
GTCAGGAACAATCTTACGATCCCCACAGCGGTCAGACAGCTCCTGGCTA
CTCAGAATCCAGTGAATACGAACATAGCGGAGACTACGATAACTCCCAG
AACCAGCAATATTCCTCAACTCCCTCTAACGCTAACGTTAACCTAATCGA
5 CCAGTATCTCCATCTAATCCAATTACATAGCATCCCATCCGATTTAGTCC
AATACGCCGAATCCTACTTAACACACGCCAAGAAGTCCATCCGATACTA
CGCCGTGCACGCCAAGGACTTTGAGAGGATTCGACCCTGCCTTGAATCC
GTCACGAAGTACTTCAATATGCTCAATGACGATCTCGCCAGGGAGTACG
TCAGATGTCAACGACAATGTTACCTTGATCGTCTCAATAGCTACACAACG
10 GCTATCTCTCAGTATACTGTCACCACAAATGCCTGCATAAACAACCGTTT
GAACTGAAGATGAGGCTTTTTTTGTGAAATATTTATTTGGGTCAGTGAAA
ATAAATTTTCATCAACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PERM-P2-G11 (SEQ ID NO:70)

15 AGTATTCAGTTGTTAGAGATCTTTCCAACATGATATTGAAATTGTGCGCC
ATTGCGGTTTTATTTTTCCTTATTGGAGACGGAGAAGCAGCTCCTAGACC
AACAAGATTCATCCCTTTTCGCTATCATCTCAGATCTGCACAGGAAGGCCA
TGCACGACGAAAAGAACAGATTTACTAGTATAGTGAAATATGGTCAATT
GAAGTACAATGGAGAGAAATATACTCTGTCCATCAGAAGTGAGAATCTC
20 CATTATTTACAAAGGACACCTACAAAGGAACCGGAGCCGATATGTCCG
AGTTGATCTACTTCAATGACAAGCTCTACACTCTTAACGACGAAACAGG
AACTATCTATGAGGTGAAACACGGCGGAGAGCTCATTCCATGGATAACT
CTCAAGAATGACGATGGAAATCAAAGGACGGCTTCAAAGCTAAATGG
GCAACAGTTAAGGGTAACAAGTTGATTGTCGGATCAGCAGGAATGGCCT
25 TTCTGGACGCGAAAACCATGAATATTGACAGAGACGCCCTCTGGGTGAA
GGAAATCAGCGAATCTGGCCACGTCACATAAATATTGGGATAGTCAA
TACAAGAAAGTGAGGGACGCCATGGGACTCGTCTCCGGATTTGTCTGGC
ATGAGGCCGTAAATTGGTCACCAAGGAAGAATCTTTGGGTCTTCATGCC
CAGGAAATGCACAAATGAACCATATACCGTTCGCTTAGACAAGAAAACC
30 GGATGCAATCAGATTATCACGGCCAATGAAAACCTCAATGATGTTAGAG
CAATTCATATCAATCGAGCCGCTGCAGATCCAGCTTCTGGATTCTCCTCT
TTCAAGTTCATCCCAAACACCAGAAACAATGATATCTTCGCAATCAAGA

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CAATCGAGAGGAACGGCCAAACAGCCACTTATGGCACAGTGATTGACAT
CAATGGGAAGACTTTGTTGCCCGATCAGCGAATTCTCGATGATAAATAT
GAAGGAATTGCATTTTTCAAGGATCCCAAAGGAATTAAGTAAAGATGGA
TTATAAAATGTTGAAATAAAATGTCATGAAGCTTATAAAATGAAAAAAA
5 AAAAAAAAAAAAAAAAAAAAAA

PERM-P5-E2 (SEQ ID NO:72)

AGTTCAGTTTTCTGTGGAAAATGAATACCTTATTGAAAGTCGCGGTTTTG
CTAAGCTTGGGAGGAACTGGGTACTCTTGGCAATATCCCAGGAATGCCG
10 ATCAAACCTCTCTGGGCTTGGAGATCGTGTCAAAGGAGCACATCGGCGA
CGACCAAGCATTATTGAAGAAATGGTTGAAATTTGAAATTCCAGATGAT
AAAGTAACGCATTGTTTTATTAAATGTACTTGGATCCATTTAGGAATGTA
CGATGAAAAAACTAAAACCATTAGGGTTGATAAGGTCAAGCAACAATTC
GAGGGACGCAAATTACCAGTTCCTGCTGAAATCAGCAAATTAGAGGGTC
15 CTACAGATGGCGATTGTGAAAAAATTTACAGAAAACTAAGGCTTTTCT
TGACGCTCAAATGAAGAATTATCGCATTGCATTCTATGGCATTATGATG
GATCCGATGCATGGTTTGCAGAACATCCCGAACTAAGCCCAAGAAAAC
GAAGATTTCTGAATTCTGCAAAGGTCGTGAAGGTGGAAAGGAAGGAAC
TGCAAGCATGCTTGCAGCATGTACTACTACCGCTTAGTCGATGAGGATA
20 ATCTTGTGATTCCCTTCAGGAAGTTGCCAGGCATCTCAGAGTCTGATCT
TAAACAATGCAGAGATGCCGCTAGCAAGAAAAGTGGATGCCAAGTTGCT
GATGACAATCTACGATTGTCTTAACAAGATCAACCCGACAGGTCTTAAA
ACTGCTTTAAATACGCTCGATGAGCAATCATTAAACAATTATTAGAAAA
GAAATAAAAATTGATTTTCGAGCAATCGTAAAAAAAAAAAAAAAAAAAAA
25 AAAAAAAAAA

PERM-P5-C11 (SEQ ID NO:74)

ATCATTAGTGAAGTTGTTAACAATAAGCATGAAGTACTTTTCTCTCAAT
TTTCTTCTAATTGTGATTCTATTGATTGTGGCTTGTTACCTCAATTACCA
30 TGTTTACCCAGGATTCCAAGAAAAAGCCGTCCAATCCTCGTCCTAAATT
ATCGGCCAGAAGTGGTTTGTCTTATTGAGTTATCACACTAGGAATTCGAT
GCAGTAATTTATTACGTGGGCATTGTGGCTTCATAGCTGGGGCCGTAAAA

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ATTAAAAGACAAAAAGAAATTATTACATGACGGCCGCCATAAGTCGACG
AAAATGGACATAACATCCTTGACTACCTATCGTAATGTGAATTTGAAAA
ATTATACAAAAAATAATTATGAATTAGCAAAAAATAAAAATTATCAGAG
GAGCAGATCTGCTGTTATGATTTCTTTTTATGTCTCTTTTATGTAAGCAAT
5 CACTATTCTTGTACGAATATATAAATAAAAGTTCCAAGTGTGTCAAAAAA
AAAAAAAAAAAAAAAAAAAAA

PERM-P5-H8 (also referred to as P2-G9) (SEQ ID NO:76)

AGTCAGTTATTGTTTCGAAAAATGAAGAAAATTGTGCTATTCAGTTTTATA
10 TTCGTTGCTTTGGTGATCAGTGCTAAAGCCATTGAGACGGAATTGGATGA
TCCCGATGATGCCACTAAAGGTCGGGATGTTGCGAAGGCAGAACCTGGA
CAACTGGGACAAGTTCCAGTTGTACCTGATTTAAATCCTTCGAACACGAG
GAAACGGAGGAATAGATCCAGAAAAAGGCGACGAAATCTAGGAAAGAG
ACTCAAAAAAGTTTTTGCATAGAAATTAATACTAAAAAGATTAAACTA
15 TGTCAATTTGATGCCTTTTGAGCATTCAATTA AAAAGTATGACAAATTAT
TAAGAAAAAAAAAAAAAAAAAAAAAAAAA

PERL-P3-B3 (SEQ ID NO:78)

ACTTAATATTGGACTGTATTTTGAGATAGACACCCAGAGTACGATGGTG
20 CAATGTGAATTCGGTGGAACACCTTGTACGACTTTGAATATTTTCATATCC
AACGATCAAGCCACTGGTGAATGCCTGAGTGTTGTGTTGAGCTCAGTCG
CGGTGGAGCAGCGAGCCGAGAAAGAATGGCAAAGGTGCAATAGAGATA
CTAAACTAGAGGAAAGACTTGAACGGTGACAGAGGAATAGGAGCAAGA
AAGAAGTGTTGAGAATTTGCGGGAATTTCTATGGCCAATATTAAGTGTTG
25 ATTCAAAGAGTTTTCTACACAGAGAAATTGCGAGGTCAC TTATTGGAAA
TCAATGAGAAAGTTTTTAATGTTTTTCGTGAAAGGAGTGAATAAAAATTG
AGTGCTTTATACATGTGAGACTCCCCCTTTCTGTGGAGAGACGATAAAA
GGAAATTCGATATTTATGGGAAAAGTGATGAATTAGTGATACTGGTGGC
TCTCGAAACACAAGTCACGAATTAGAAAACGTCCAAAGAGTGATTTTTG
30 TGCTCTCCGGTGGCTGATATAAGAGAATGTGAAGAGTGAGGATGATGTC
TCGCTGGAGCAAAAGTGTGAAATTTGTGTGCCTCCTCCTGTGTGGCGGG

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TTCACGTTTCTCACAACATCAGCACGTGCCAAACCCACGCTGACCTTTCA
GCTTCCGCCCCGCCCTCACGAACCTACCCCCCTTCATAGGCATCTCGCGAT
TTGTGGAACGCAAAATGCAGAATGACCAGATGAAGACCTACACTGGCGT
TCGGCAGACGAACGACTCTCTCGTGATGATCTACCACCATGATCTGACG
5 ATCGCCATCGTGGAATTGGGACCAGAGAAGACTCTCTTGGGTGTGAAT
TGATAGAAATTAACAACGATGATGAAGGCGCCAAAGTGCTCACAGAACT
GGCCACCGTGAATATACCACTGCAGATCGACTTCCGGGAGATGGTGAAG
CTCATGAAGCAGTGCGAGAAGATCGATTACATGCGGAAAGTGAAACGCC
AGGGAGCATCAGAGAGTGACCAGACAACAAATCGTCAACATCAGACGG
10 GCTACTTTGGACTCGGAGGCGCCACCGCCGGTCTAAGCATCCTCAGTGG
CATCCTTCCCGGCACCAAGTGGTGTGGCACAGGAGACATCGCCAAAACA
TACCACGATCTCGGCACCGAGGCCACTATGGACATGTGCTGTGCACTC
ATGATCTCTGTCCAGTGAAAGTGCGCTCATATCAGCAGCGCTACAATCTC
AGCAATAACTCTATCTACACAAAATCTCCCTGCAAATGTGATGACATGCT
15 GTTCAATTGCCTCAAGAGGACCAACACGTCAGCCTCGCAATTCATGGGG
ACCATCTACTTCAACGTGGTCCAAGTGCCATGTGTTCTGGACACAGAGA
GAGGCTACAGATTCAGAAAAGCGAGAACCTTCTCCTGAGTATTGCAAAA
CAACGAAATCTGCGGATTTTTTTTTTATTTTTGGGACTTTTCGTGTGTAAAG
ACCATTTCTTGTGATTTTCAGCTGCGGTGCTCTTTCAAATGAATTATTTAT
20 GTTGCTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PERM-P2-D11 (SEQ ID NO:80)

GTATTAGAAAACCAATCATGAAGCAGCTTGTTGTATTTTTGGCGTTGATA
GTTCTAATAGTGATTTGTACGCAAAACGACCTTCGAGGAAGTGTAGGA
25 GTGGAATGGTGAAAGAGGAAGAGTGTATACTCCATTGTGAGTACAAATA
TTATGGCTTTACCGATGATAAGTTCCAACCTTGATGCAGATCAGAGAGGA
AACTTTAGATTTGCCATGATGGACTATGGAGCAATTAGGATGGATCAGG
AGGGTCAAATGGATGAGCATTGAAAAAATGTGCCAATGAAGCTGAAAA
GGCTCCAGTGTGCTCCAAGGTGGATAAGTGTAGGAAAATCATTAGTAC
30 TATCGCTGTGCAGTGAATAATAAACTTTTCCAATATAATGCTTATGCCAA
AGCAATTATTGCGCTTGATAAGACAATTAATGTTTAAAAAGTGGAATGA

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ATCCCTAAAATAAAGAAGGAAAGATAAGAAGCTTTCAAGAAAAGCTTGAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAA

PERM-P5-E3 (SEQ ID NO:82)

5 ACACACATACGATTCATTACCAGAAATGAAGCAGTTACCAAGTGATCCTT
CTGGCCTTAGTCTTTCTGATCGCAAAATGTGATCAGAAAAACCGGAAT
ATAAGTGCCGCAGAGACTTCAAGACCGAGGATAAAAATTGCTTCCTTTC
TTGTACATTTAAAAATTACCACTTCATTGATAACAAGTTCAGGATTGAAA
GGAAGAATATTGAAAAGTACAAGAAGTTCATAACTGACTATAAGGCCCT
10 GAAACCCAATGTTAGCGATAATGATTTGGAAAAACACCTGTTGGATTGT
TGGGATAAATTCAAAAATCACCTGAAGCATCAACAAGGCCCGAAAAAT
GTGAAAAAGTCAACAAGTTTGAAGATGTGTTATTGACAAGAATATCTT
TGATTATCCTATTTACTTCAATGCTTTGAAGAAAATAAATTACATTACAA
AGGTTTAATGAAAAATTGATGAAATAAACATAATGAATTATTGCATTGA
15 ATAACAAAAAAAAAAAAAAAAAAAAAAAAAAAA

PERM-P2-F11 (SEQ ID NO:84)

AGTTATTGTTGGGAAAATGAAGAAAATTGTGCTGTTCAAGTGTTATATTCA
TTGCTTTGGTGATCAGTGCTAAAGCCATTG
20 AGGATGAGGATGATGATGATGACGATGATGAATCTGAAGATCGG
GATGTTGCGAGGGCAGAACGTGAACAACAGGAAGAAGAACCAGACGAA
CCTGAATATATTCCTTCTAGACCGAGGAATCGGTCGAAAATGAGAAAAT
GGAGGAATAGAACTATAGAAAATATAGAGACGAAAGTAGGAAAAGAA
AGCGAGATATGGTTTTGGATGTTATCAGAAGATTTTATAGAAATTAATA
25 CTAAAAGTATTAAGTGGATCAATTTGATGCCTTTTGAGTGATTCATTTG
AACTTTGAAAAATAAAACAAAGAATGTAAAAAAAAAAAAAAAAAAAAA
AAAAAAA

Also included are fragments of the above-described nucleic acid sequences
that are at least 33 bases, at least 36 bases, at least 42 bases or at least 48 bases in
30 length, which is sufficient to permit the fragment to selectively hybridize to a
polynucleotide that encodes a disclosed *P. ariasi* polypeptide or that encodes a
disclosed *P. perniciosus* polypeptide under physiological conditions. The term

“selectively hybridize” refers to hybridization under moderately or highly stringent conditions, which excludes non-related nucleotide sequences.

Also disclosed herein are open reading frames (ORFs) encoding a *P. ariasi* or a *P. perniciosus* polypeptide. These ORFs are delimited by a start codon and by a stop codon. This also includes the degenerate variants and nucleotide sequences encoding conservative variants and homologs. Specific, non-limiting examples of ORFs encoding a *P. ariasi* or a *P. perniciosus* polypeptide include a nucleic acid sequence from position 104 to position 1444 (104-1444) of SEQ ID NO:2, 4-759 of SEQ ID NO:4, 23-1189 of SEQ ID NO:6, 19-1200 of SEQ ID NO:8, 23-901 of SEQ ID NO:10, 25-963 of SEQ ID NO:12, 21-1148 of SEQ ID NO:14, 22-438 of SEQ ID NO:16, 24-1190 of SEQ ID NO:18, 29-787 of SEQ ID NO:20, 34-375 of SEQ ID NO:22, 19-852 of SEQ ID NO:24, 73-822 of SEQ ID NO:26, 40-1041 of SEQ ID NO:28, 29-442 of SEQ ID NO:30, 53-565 of SEQ ID NO:32, 29-781 of SEQ ID NO:34, 45-182 of SEQ ID NO:36, 85-783 of SEQ ID NO:38, 26-223 of SEQ ID NO:40, 69-413 of SEQ ID NO:42, 70-945 of SEQ ID NO:44, 19-438 of SEQ ID NO:46, 15-428 of SEQ ID NO:48, 46-1227 of SEQ ID NO:49, 5-1171 of SEQ ID NO:51, 25-651 of SEQ ID NO:53, 63-995 of SEQ ID NO:55, 55-1350 of SEQ ID NO:57, 16-411 of SEQ ID NO:59, 29-1195 of SEQ ID NO:61, 43-792 of SEQ ID NO:63, 66-776 of SEQ ID NO:65, 73-846 of SEQ ID NO:67, 30-1025 of SEQ ID NO:69, 21-713 of SEQ ID NO:71, 30-179 of SEQ ID NO:73, 21-269 of SEQ ID NO:75, 584-1465 of SEQ ID NO:77, 18-431 of SEQ ID NO:79, 26-451 of SEQ ID NO:81, 17-310 of SEQ ID NO:83.

In several embodiments:

The PRL-P4-A10 mature protein is 426 amino acids long (21-446 of SEQ ID NO:1) and is encoded by the nucleic acid sequence 164-1441 of SEQ ID NO:2.

The PRL-P4-A9 mature protein is 232 amino acids long (20-251 of SEQ ID NO:3) and is encoded by the nucleic acid sequence 61-756 of SEQ ID NO:4.

The PRL-P4-C10 mature protein is 370 amino acids long (19-388 of SEQ ID NO:5) and is encoded by the nucleic acid sequence 77-1186 of SEQ ID NO:6.

The PRL-P4-D6 mature protein is 375 amino acids long (19-393 of SEQ ID NO:7) and is encoded by the nucleic acid sequence 73-1197 of SEQ ID NO:8.

The PRL-P4-D7 mature protein is 275 amino acids long (18-292 of SEQ ID NO:9) and is encoded by the nucleic acid sequence 74-898 of SEQ ID NO:10.

The PRL-P4-E5 mature protein is 290 amino acids long (23-312 of SEQ ID NO:11) and is encoded by the nucleic acid sequence 91-960 of SEQ ID NO:12.

5 The PRL-P4-F3 mature protein is 350 amino acids long (26-375 of SEQ ID NO:13) and is encoded by the nucleic acid sequence 96-1145 of SEQ ID NO:14.

The PRL-P4-G12 mature protein is 118 amino acids long (21-138 of SEQ ID NO:15) and is encoded by the nucleic acid sequence 82-435 of SEQ ID NO:16.

10 The PRL-P4-G7 mature protein is 365 amino acids long (24-388 of SEQ ID NO:17) and is encoded by the nucleic acid sequence 93-1187 of SEQ ID NO:18.

The PRL-P6-E11 mature protein is 234 amino acids long (19-252 of SEQ ID NO:19) and is encoded by the nucleic acid sequence 83-784 of SEQ ID NO:20.

The PRM-P3-A6 mature protein is 93 amino acids long (21-113 of SEQ ID NO:21) and is encoded by the nucleic acid sequence 94-372 of SEQ ID NO:22.

15 The PRM-P3-F11 mature protein is 258 amino acids long (20-277 of SEQ ID NO:23) and is encoded by the nucleic acid sequence 76-849 of SEQ ID NO:24.

The PRM-P5-D6 mature protein is 228 amino acids long (22-249 of SEQ ID NO:25) and is encoded by the nucleic acid sequence 136-819 of SEQ ID NO:26.

20 The PRM-P5-E9 mature protein is 313 amino acids long (21-333 of SEQ ID NO:27) and is encoded by the nucleic acid sequence 100-1038 of SEQ ID NO:28.

The PRM-P5-F12 mature protein is 116 amino acids long (22-137 of SEQ ID NO:29) and is encoded by the nucleic acid sequence 92-439 of SEQ ID NO:30.

The PRM-P5-F2 mature protein is 150 amino acids long (21-170 of SEQ ID NO:31) and is encoded by the nucleic acid sequence 113-562 of SEQ ID NO:32.

25 The PRM-P5-G11 mature protein is 231 amino acids long (20-250 of SEQ ID NO:33) and is encoded by the nucleic acid sequence 86-778 of SEQ ID NO:34.

The PRM-P5-H4 mature protein is 21 amino acids long (25-45 of SEQ ID NO:35) and is encoded by the nucleic acid sequence 117-179 of SEQ ID NO:36.

30 The PRS-P1-B11 mature protein is 215 amino acids long (18-232 of SEQ ID NO:37) and is encoded by the nucleic acid sequence 136-780 of SEQ ID NO:38.

The PRS-P1-B4 mature protein is 45 amino acids long (21-65 of SEQ ID NO:39) and is encoded by the nucleic acid sequence 86-220 of SEQ ID NO:40.

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The PRS-P1-E7 mature protein is 93 amino acids long (22-114 of SEQ ID NO:41) and is encoded by the nucleic acid sequence 132-410 of SEQ ID NO:42.

The PRS-P1-G9 mature protein is 262 amino acids long (30-291 of SEQ ID NO:43) and is encoded by the nucleic acid sequence 157-942 of SEQ ID NO:44.

5 The PRS-P2-C8 mature protein is 119 amino acids long (21-139 of SEQ ID NO:45) and is encoded by the nucleic acid sequence 79-435 of SEQ ID NO:46.

The PRS-P2-G8 mature protein is 118 amino acids long (20-137 of SEQ ID NO:47) and is encoded by the nucleic acid sequence 72-425 of SEQ ID NO:48.

10 The PERL-P7-G8 mature protein is 375 amino acids long (19-393 of SEQ ID NO:49) and is encoded by the nucleic acid sequence 100-1224 of SEQ ID NO:50.

The PERL-P6-H9 mature protein is 370 amino acids long (19-388 of SEQ ID NO:51) and is encoded by the nucleic acid sequence 59-1168 of SEQ ID NO:52.

The PERL-P7-C2 mature protein is 191 amino acids long (18-208 of SEQ ID NO:53) and is encoded by the nucleic acid sequence 76-648 of SEQ ID NO:54.

15 The PERL-P6-H1 mature protein is 282 amino acids long (29-310 of SEQ ID NO:55) and is encoded by the nucleic acid sequence 147-992 of SEQ ID NO:56.

The PERL-P3-E11 mature protein is 411 amino acids long (21-431 of SEQ ID NO:57) and is encoded by the nucleic acid sequence 115-1347 of SEQ ID NO:58.

20 The PERL-P7-G12 mature protein is 112 amino acids long (20-131 of SEQ ID NO:59) and is encoded by the nucleic acid sequence 73-408 of SEQ ID NO:60.

The PERL-P3-C9 mature protein is 365 amino acids long (24-388 of SEQ ID NO:61) and is encoded by the nucleic acid sequence 98-1192 of SEQ ID NO:62.

25 The PERM-P2-A10 mature protein is 230 amino acids long (20-249 of SEQ ID NO:63) and is encoded by the nucleic acid sequence 100-789 of SEQ ID NO:64.

The PERL-P6-H11 mature protein is 217 amino acids long (20-236 of SEQ ID NO:65) and is encoded by the nucleic acid sequence 123-773 of SEQ ID NO:66.

The PERS-P1-H11 mature protein is 232 amino acids long (26-257 of SEQ ID NO:67) and is encoded by the nucleic acid sequence 148-843 of SEQ ID NO:68.

30 The PERM-P2-G11 mature protein is 311 amino acids long (21-331 of SEQ ID NO:69) and is encoded by the nucleic acid sequence 90-1022 of SEQ ID NO:70.

The PERM-P5-E2 mature protein is 211 amino acids long (20-230 of SEQ ID NO:71) and is encoded by the nucleic acid sequence 78-710 of SEQ ID NO:72.

The PERM-P5-C11 mature protein is 24 amino acids long (26-49 of SEQ ID NO:73) and is encoded by the nucleic acid sequence 105-176 of SEQ ID NO:74.

5 The PERM- P5-H8 (also referred to P2-G9) mature protein is 62 amino acids long (21-82 of SEQ ID NO:75) and is encoded by the nucleic acid sequence 81-266 of SEQ ID NO:76.

The PERL-P3-B3 mature protein is 264 amino acids long (30-293 of SEQ ID NO:77) and is encoded by the nucleic acid sequence 671-1462 of SEQ ID NO:78.

10 The PERM-P2-D11 mature protein is 118 amino acids long (20-137 of SEQ ID NO:79) and is encoded by the nucleic acid sequence 75-428 of SEQ ID NO:80.

The PERM-P5-E3 mature protein is 121 amino acids long (21-141 of SEQ ID NO:81) and is encoded by the nucleic acid sequence 86-448 of SEQ ID NO:82.

15 The PERM-P2-F11 mature protein is 77 amino acids long (21-97 of SEQ ID NO:83) and is encoded by the nucleic acid sequence 77-307 of SEQ ID NO:84.

Another specific, non-limiting example of a polynucleotide encoding a *P. ariasi* polypeptide is a polynucleotide having at least 75%, 85%, 90%, 95%, or 99% homologous to one of the sequences set forth above that encodes a polypeptide having an antigenic epitope or function of a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide. Yet another specific, non-limiting example of a polynucleotide encoding a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide is a polynucleotide that encodes a polypeptide that is specifically bound by an antibody that specifically binds the *P. ariasi* polypeptide or the *P. perniciosus* polypeptide.

25 The *P. ariasi* polynucleotides and *P. perniciosus* polynucleotides include a recombinant DNA which is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (e.g., a cDNA) independent of other sequences. The nucleotides can be ribonucleotides, deoxyribonucleotides, or modified forms of either nucleotide. The term includes single and double forms of DNA.

30 Recombinant vectors are also disclosed herein that include a polynucleotide encoding a polypeptide or a fragment thereof according to the disclosure.

Recombinant vectors include plasmids, viral vectors, and bacterial vectors and may be used for *in vitro* or *in vivo* expression.

A plasmid may include a DNA transcription unit, a nucleic acid sequence that permit it to replicate in a host cell, such as an origin of replication (prokaryotic or eukaryotic). A plasmid may also include one or more selectable marker genes
5 and other genetic elements known in the art. Circular and linear forms of plasmids are encompassed in the present disclosure.

For *in vivo* expression, the promoter is generally of viral or cellular origin. In one embodiment, the cytomegalovirus (CMV) early promoter (CMV-IE promoter), including the promoter and enhancer, is of use. The CMV-IE promoter
10 can be of human or murine origin, or of other origin such as rat or guinea pig (see EP 0260148; EP 0323597; WO 89/01036; Pasleau *et al.*, *Gene* 38:227-232, 1985; Boshart M. *et al.*, *Cell* 41:521-530, 1985). Functional fragments of the CMV-IE promoter may also be used (WO 98/00166). The SV40 virus early or late promoter
15 and the Rous Sarcoma virus LTR promoter are also of use. Other promoters include but are not limited to, a promoter of the cytoskeleton gene, such as (but not limited to) the desmin promoter (Kwissa M. *et al.*, *Vaccine* 18(22):2337-2344, 2000), or the actin promoter (Miyazaki J. *et al.*, *Gene* 79(2):269-277, 1989). When several genes are present in the same plasmid, they may be provided in the same transcription unit
20 or in different units.

The plasmids may also comprise other transcription regulating elements such as, for example, stabilizing sequences of the intron type. In several embodiments the plasmids include the first intron of CMV-IE (WO 89/01036), the intron II of the rabbit β -globin gene (van Ooyen *et al.*, *Science* 206: 337-344, 1979), the signal
25 sequence of the protein encoded by the tissue plasminogen activator (tPA; Montgomery *et al.*, *Cell. Mol. Biol.* 43:285-292, 1997), and/or a polyadenylation signal (polyA), in particular the polyA of the bovine growth hormone (bGH) gene (US-A-5,122,458) or the polyA of the rabbit β -globin gene or of SV40 virus.

In a specific, non-limiting example, the pVR1020 plasmid (VICAL Inc.;
30 Luke C. *et al.*, *Journal of Infectious Diseases* 175:91-97, 1997; Hartikka J. *et al.*, *Human Gene Therapy* 7:1205-1217, 1996)) can be utilized as a vector for the insertion of such a polynucleotide sequence, generating recombinant plasmids such

as, but not limited to, PJV001, PJV002, PJV003, PJV004, PJV005, PJV006, PJV007, PJV008, PJV009, PJV010, PJV011, PJV012, PJV013, PJV014, PJV015, PJV016, PJV017, PJV018, PJV019, PJV020, PJV021, PJV022, PJV023, PJV024, PJV025, PJV026, PJV027, PJV028, PJV029, PJV030, PJV031, PJV032, PJV033, 5 PJV034, PJV035, PJV036, PJV037, PJV038, PJV039, PJV040, PJV041, or PJV042. The plasmids are evaluated in dogs in order to determine their efficacy against a Leishmania infection (Vidor E. et al., P3.14, XXIV World Veterinary Congress, Rio de Janeiro, Brazil, 18-23 August 1991).

Various viral vectors are also of use with a polynucleotide encoding a *P. ariasi* or a *P. perniciosus* polypeptide. A specific, non-limiting example includes 10 recombinant poxvirus, including avipox viruses, such as the canarypox virus. Another specific, non-limiting example includes vaccinia viruses (U.S. Patent No. 4,603,112), such as attenuated vaccinia virus such as NYVAC (see U.S. Patent No. 5,494,807) or Modified Vaccinia virus Ankara (MVA, Stickl H. and Hochstein- 15 Mintzel V., *Munch. Med. Wschr.* 113:1149-1153, 1971; Sutter G. et al., *Proc. Natl. Acad. Sci. U.S.A.* 89:10847-10851, 1992; Carroll M. W. et al., *Vaccine* 15(4):387-394, 1997; Stittelaar K. J. et al., *J. Virol.* 74(9):4236-4243, 2000; Sutter G. et al., *Vaccine* 12(11):1032-1040, 1994). When avipox viruses are used, canarypox viruses (U.S. Patent No. 5,756,103) and fowlpox viruses (U.S. Patent No. 20 5,766,599) are of use, such as attenuated viruses. For recombinant canarypox virus vectors, the insertion sites may be in particular in the ORFs C3, C5 or C6. When the expression vector is a poxvirus, the heterologous polynucleotide can be inserted under the control of a poxvirus specific promoter, such as the vaccinia virus 7.5kDa promoter (Cochran et al., *J. Virology* 54:30-35, 1985), the vaccinia virus I3L 25 promoter (Riviere et al., *J. Virology* 66:3424-3434, 1992), the vaccinia virus HA promoter (Shida, *Virology* 150:451-457, 1986), the cowpox virus ATI promoter (Funahashi et al., *J. Gen. Virol.* 69:35-47, 1988), other vaccinia virus H6 promoter (Taylor et al., *Vaccine* 6:504-508, 1988; Guo et al., *J. Virol.* 63:4189-4198, 1989; Perkus et al., *J. Virol.* 63:3829-3836, 1989).

30 Other viral vectors of use are herpes virus or adenovirus vectors. Specific, non-limiting examples include a canine herpes virus (CHV) or canine adenovirus (CAV) vector (for example, see U.S. Patent No. 5,529,780; U.S. Patent No.

5,688,920; Published PCT Application No. WO 95/14102). For CHV, the insertion sites may be in particular in the thymidine kinase gene, in the ORF3, or in the UL43 ORF (see U.S. Patent No. 6,159,477). For CAV, the insertion sites may be in particular in the E3 region or in the region located between the E4 region and the right ITR region (see U.S. Patent No. 6,090,393; U.S. Patent No. 6,156,567). In one embodiment in CHV or CAV vectors the insert is in general under the control of a promoter (as described above for the plasmids), such as CMV-IE promoter.

Multiple insertions can be done in the same vector using different insertion sites or using the same insertion site. When the same insertion site is used, each polynucleotide insert is inserted under the control of different promoters. The insertion can be done tail-to-tail, head-to-head, tail-to-head, or head-to-tail. IRES elements (Internal Ribosome Entry Site, see European Patent EP 0803573) can also be used to separate and to express multiple inserts operably linked to the same promoter. Bacterial vectors may also be used for *in vivo* expression.

Any polynucleotide according to the disclosure can be expressed *in vitro* by DNA transfer or expression vectors into a suitable host cell. The host cell may be prokaryotic or eukaryotic. The term "host cell" also includes any progeny of the subject host cell. Methods of stable transfer, meaning that the foreign polynucleotide is continuously maintained in the host cell, are known in the art. Host cells can include bacteria (e.g. *Escherichia coli*), yeast, insect cells, and vertebrate cells. Methods of expressing DNA sequences in eukaryotic cells are well known in the art.

As a method for *in vitro* expression, recombinant Baculovirus vectors (e.g., Autographa California Nuclear Polyhedrosis Virus (AcNPV)) can be used with the nucleic acids disclosed herein. For example, polyhedrin promoters can be utilized with insect cells (for example *Spodoptera frugiperda* cells, like Sf9 available at the ATCC under the accession number CRL 1711, Sf21) (see for example, Smith *et al.*, *Mol. Cell Biol.* 3:2156-2165, 1983; Pennock *et al.*, *Mol. Cell Biol.* 4: 399-406, 1994; Vialard *et al.*, *J. Virol.* 64:37-50, 1990; Verne A., *Virology* 167:56-71, 1988; O'Reilly *et al.*, "Baculovirus expression vectors, A laboratory manual," New York Oxfore, Oxfore University Press, 1994; Kidd I. M. & Emery V.C., "The use of baculoviruses as expression vectors," *Applied Biochemistry and Biotechnology*

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42:37-159, 1993; European Patent No. EP 0370573; European Patent No. EP 0265785; U.S. Patent No. 4,745,051). For expression the BaculoGold™ Starter Package (Cat # 21001K) from Pharmingen (Becton Dickinson) can be used.

5 As a method for *in vitro* expression, recombinant *E. coli* can be used with a vector. For example, when cloning in bacterial systems, inducible promoters such as arabinose promoter, pL of bacteriophage lambda, plac, ptrp, ptac (ptrp-lac hybrid promoter), and the like may be used.

10 Transformation of a host cell with recombinant DNA may be carried out by conventional techniques as are well known to those skilled in the art. Where the host is prokaryotic, such as *E. coli*, competent cells which are capable of DNA uptake can be prepared from cells harvested after exponential growth phase and subsequently treated by the CaCl₂ method using procedures well known in the art. Alternatively, MgCl₂ or RbCl can be used. Transformation can also be performed after forming a protoplast of the host cell if desired, or by electroporation.

15 When the host is a eukaryote, methods of transduction of DNA such as calcium phosphate coprecipitates, conventional mechanical procedures such as microinjection, electroporation, insertion of a plasmid encased in liposomes, or virus vectors may be used. Eukaryotic cells can also be cotransformed with *P. ariasi* polynucleotide sequences or *P. perniciosus* polynucleotide sequences, and a second foreign DNA molecule encoding a selectable phenotype, such as the herpes simplex thymidine kinase gene. Another method is to use a eukaryotic viral vector (see above), such as a herpes virus or adenovirus (for example, canine adenovirus 2), to transiently transduce eukaryotic cells and express the protein (see for example, Eukaryotic Viral Vectors, Cold Spring Harbor Laboratory, Gluzman ed., 1982).

25 Isolation and purification of recombinantly expressed polypeptides may be carried out by conventional means including preparative chromatography (e.g., size exclusion, ion exchange, affinity), selective precipitation and ultra-filtration. Such a recombinantly expressed polypeptide is part of the present disclosure. The methods for production of such a polypeptide are also encompassed, in particular the use of a host cell and a recombinant expression vector comprising a polynucleotide according to the disclosure.

30

Antibodies

A polypeptide of the disclosure or a fragment thereof according to the disclosure can be used to produce antibodies. Polyclonal antibodies, antibodies which consist essentially of pooled monoclonal antibodies with different epitopic
5 specificities, as well as distinct monoclonal antibodies are included. Without being bound by theory, antibodies are of use as markers for exposure, and as immunodiagnostic tools to follow the development of the immune response to *Phlebotomus* salivary proteins.

The preparation of polyclonal antibodies is well-known to those skilled in
10 the art. See, for example, Green *et al.*, "Production of Polyclonal Antisera," *Immunochemical Protocols*, pp. 1-5, Manson, ed., *Humana Press*, 1992; Coligan *et al.*, "Production of Polyclonal Antisera in Rabbits, Rats, Mice and Hamsters," *Current Protocols in Immunology*, section 2.4.1, 1992.

The preparation of monoclonal antibodies likewise is conventional. See, for
15 example, Kohler & Milstein, *Nature* 256:495, 1975; Coligan *et al.*, sections 2.5.1-2.6.7; and Harlow *et al.*, *Antibodies: A Laboratory Manual*, p. 726, Cold Spring Harbor Pub., 1988. Briefly, monoclonal antibodies can be obtained by injecting mice with a composition comprising an antigen, verifying the presence of antibody production by removing a serum sample, removing the spleen to obtain B
20 lymphocytes, fusing the B lymphocytes with myeloma cells to produce hybridomas, cloning the hybridomas, selecting positive clones that produce antibodies to the antigen, and isolating the antibodies from the hybridoma cultures. Monoclonal antibodies can be isolated and purified from hybridoma cultures by a variety of well-established techniques. Such isolation techniques include affinity chromatography
25 with Protein-A Sepharose, size-exclusion chromatography, and ion-exchange chromatography. See, *e.g.*, Coligan *et al.*, sections 2.7.1-2.7.12 and sections 2.9.1-2.9.3; Barnes *et al.*, "Purification of Immunoglobulin G (IgG)," *Methods in Molecular Biology*, Vol. 10, pages 79-104, Humana Press, 1992.

Methods of *in vitro* and *in vivo* multiplication of monoclonal antibodies are
30 well known to those skilled in the art. Multiplication *in vitro* may be carried out in suitable culture media such as Dulbecco's Modified Eagle Medium or RPMI 1640 medium, optionally supplemented by a mammalian serum such as fetal calf serum or

trace elements and growth-sustaining supplements such as normal mouse peritoneal exudate cells, spleen cells, thymocytes, or bone marrow macrophages. Production *in vitro* provides relatively pure antibody preparations and allows scale-up to yield large amounts of the desired antibodies. Large-scale hybridoma cultivation can be carried out by homogenous suspension culture in an airlift reactor, in a continuous stirrer reactor, or in immobilized or entrapped cell culture. Multiplication *in vivo* may be carried out by injecting cell clones into mammals histocompatible with the parent cells, *e.g.*, syngeneic mice, to cause growth of antibody-producing tumors. In one embodiment, the animals are primed with a hydrocarbon, especially oils such as pristane (tetramethylpentadecane) prior to injection. After one to three weeks, the desired monoclonal antibody is recovered from the body fluid of the animal.

Antibodies can also be derived from subhuman primates. General techniques for raising therapeutically useful antibodies in baboons can be found, for example, in WO 91/11465, 1991, and Losman *et al.*, *Int. J. Cancer* 46:310, 1990.

Alternatively, an antibody that specifically binds a polypeptide can be derived from a humanized monoclonal antibody. Humanized monoclonal antibodies are produced by transferring mouse complementarity determining regions from heavy and light variable chains of the mouse immunoglobulin into a human variable domain, and then substituting human residues in the framework regions of the murine counterparts. The use of antibody components derived from humanized monoclonal antibodies obviates potential problems associated with the immunogenicity of murine constant regions. General techniques for cloning murine immunoglobulin variable domains are described, for example, by Orlandi *et al.*, *Proc. Nat'l Acad. Sci. USA* 86:3833, 1989. Techniques for producing humanized monoclonal antibodies are described, for example, by Jones *et al.*, *Nature* 321:522, 1986; Riechmann *et al.*, *Nature* 332:323, 1988; Verhoeyen *et al.*, *Science* 239:1534, 1988; Carter *et al.*, *Proc. Nat'l Acad. Sci. USA* 89:4285, 1992; Sandhu, *Crit. Rev. Biotech.* 12:437, 1992; and Singer *et al.*, *J. Immunol.* 150:2844, 1993.

Antibodies can be derived from human antibody fragments isolated from a combinatorial immunoglobulin library. See, for example, Barbas *et al.*, *Methods: a Companion to Methods in Enzymology*, Vol. 2, p. 119, 1991; Winter *et al.*, *Ann. Rev. Immunol.* 12:433, 1994. Cloning and expression vectors that are useful for

producing a human immunoglobulin phage library can be obtained, for example, from STRATAGENE Cloning Systems (La Jolla, CA).

In addition, antibodies can be derived from a human monoclonal antibody. Such antibodies are obtained from transgenic mice that have been "engineered" to produce specific human antibodies in response to antigenic challenge. In this technique, elements of the human heavy and light chain loci are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the endogenous heavy and light chain loci. The transgenic mice can synthesize human antibodies specific for human antigens, and the mice can be used to produce human antibody-secreting hybridomas. Methods for obtaining human antibodies from transgenic mice are described by Green *et al.*, *Nature Genet.* 7:13, 1994; Lonberg *et al.*, *Nature* 368:856, 1994; and Taylor *et al.*, *Int. Immunol.* 6:579, 1994.

Antibodies include intact molecules as well as fragments thereof, such as Fab, F(ab')₂, and Fv which are capable of binding the epitopic determinant. These antibody fragments retain some ability to selectively bind with their antigen or receptor and are defined as follows:

(1) Fab, the fragment which contains a monovalent antigen-binding fragment of an antibody molecule, can be produced by digestion of whole antibody with the enzyme papain to yield an intact light chain (L) and a portion of one heavy chain(H);

(2) Fab', the fragment of an antibody molecule can be obtained by treating whole antibody with pepsin, followed by reduction, to yield an intact light chain and a portion of the heavy chain; two Fab' fragments are obtained per antibody molecule;

(3) (Fab')₂, the fragment of the antibody that can be obtained by treating whole antibody with the enzyme pepsin without subsequent reduction; F(ab')₂ is a dimer of two Fab' fragments held together by two disulfide bonds;

(4) Fv, defined as a genetically engineered fragment containing the variable region of the light chain (V_L) and the variable region of the heavy chain (V_H) expressed as two chains; and

(5) Single chain antibody (SCA), defined as a genetically engineered molecule containing the variable region of the light chain, the variable region of the heavy chain, linked by a suitable polypeptide linker as a genetically fused single chain molecule.

5 Methods of making these fragments are known in the art. (See for example, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, New York, 1988).

 Antibody fragments can be prepared by proteolytic hydrolysis of the antibody or by expression in *E. coli* of DNA encoding the fragment. Antibody
10 fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted F(ab')₂. This fragment can be further cleaved using a thiol reducing agent, and in one embodiment, a blocking group for the sulfhydryl groups resulting from cleavage
15 of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly (see U.S. Patents No. 4,036,945 and No. 4,331,647, and references contained therein; Nisonhoff *et al.*, *Arch. Biochem. Biophys.* **89**:230,
1960; Porter, *Biochem. J.* **73**:119, 1959; Edelman *et al.*, *Methods in Enzymology*,
20 Vol. 1, page 422, Academic Press, 1967; and Coligan *et al.* at sections 2.8.1-2.8.10 and 2.10.1-2.10.4).

 Other methods of cleaving antibodies, such as separation of heavy chains to form monovalent light-heavy chain fragments, further cleavage of fragments, or other enzymatic, chemical, or genetic techniques may also be used, so long as the
25 fragments bind to the antigen that is recognized by the intact antibody.

 For example, Fv fragments comprise an association of V_H and V_L chains. This association may be noncovalent (Inbar *et al.*, *Proc. Nat'l Acad. Sci. USA* **69**:2659, 1972). Alternatively, the variable chains can be linked by an intermolecular disulfide bond or cross-linked by chemicals such as glutaraldehyde.
30 See, e.g., Sandhu, *supra*. In one embodiment, the Fv fragments comprise V_H and V_L chains connected by a peptide linker. These single-chain antigen binding proteins (sFv) are prepared by constructing a structural gene comprising DNA sequences

encoding the V_H and V_L domains connected by an oligonucleotide. The structural gene is inserted into an expression vector, which is subsequently introduced into a host cell such as *E. coli*. The recombinant host cells synthesize a single polypeptide chain with a linker peptide bridging the two V domains. Methods for producing sFvs are known in the art (see Whitlow *et al.*, *Methods: a Companion to Methods in Enzymology*, Vol. 2, page 97, 1991; Bird *et al.*, *Science* 242:423, 1988; U.S. Patent No. 4,946,778; Pack *et al.*, *Bio/Technology* 11:1271, 1993; and Sandhu, *supra*).

Another form of an antibody fragment is a peptide coding for a single complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can be obtained by constructing genes encoding the CDR of an antibody of interest. Such genes are prepared, for example, by using the polymerase chain reaction to synthesize the variable region from RNA of antibody-producing cells (Larrick *et al.*, *Methods: a Companion to Methods in Enzymology*, Vol. 2, page 106, 1991).

Antibodies can be prepared using an intact polypeptide or fragments containing small peptides of interest as the immunizing antigen. The polypeptide or a peptide used to immunize an animal can be derived from substantially purified polypeptide produced in host cells, *in vitro* translated cDNA, or chemical synthesis which can be conjugated to a carrier protein, if desired. Such commonly used carriers which are chemically coupled to the peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid. The coupled peptide is then used to immunize an animal (*e.g.*, a mouse, a rat, or a rabbit).

Polyclonal or monoclonal antibodies can be further purified, for example, by binding to and elution from a matrix to which the polypeptide or a peptide to which the antibodies were raised is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal antibodies, as well as monoclonal antibodies (See for example, Coligan *et al.*, Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1991).

It is also possible to use the anti-idiotypic technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the

hypervariable region that is the "image" of the epitope bound by the first monoclonal antibody.

In view of the large number of methods that have been reported for attaching a variety of radiodiagnostic compounds, radiotherapeutic compounds, label (e.g.,
5 enzymes or fluorescent molecules) drugs, toxins, and other agents to antibodies one skilled in the art will be able to determine a suitable method for attaching a given agent to an antibody or other polypeptide.

In one embodiment, an antibody that binds a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide can be used to assess whether a subject has been bitten by a
10 sand fly. In one specific, non-limiting example, a sample is obtained from a subject of interest, such as a human or a dog. The sample can be a body fluid (e.g., blood, serum, urine, saliva, etc.) or a tissue biopsy. The sample or a fraction thereof is contacted with the antibody, and the ability of the antibody to form an antigen-antibody complex is assessed. One of skill in the art can readily detect the formation
15 of an antigen-antibody complex. For example, ELISA or radio-immune assays can be utilized.

Immunogenic Compositions, Vaccines and Methods of Use

Immunogenic compositions and vaccines are disclosed herein. In one
20 embodiment the immunogenic compositions and vaccines include a polypeptide. In another embodiment, the immunogenic compositions and vaccines include a recombinant vector, such as a viral vector or a plasmid. When administered to a subject such an immunogenic composition or vaccine generates an immune response to the sand fly's salivary protein(s), and surprisingly a reduction of the leishmaniasis
25 symptoms and a decrease of the leishmania parasite load. Thus, without being bound by theory, a cellular response, such as a Th1 response, produced to the salivary protein can indirectly kill a Leishmania parasite. For example, a Th1 type response can allow macrophages to take up Leishmania antigens and present them to T cells in a Th1 context. The induction of the Th1 response can produce an anti-
30 Leishmania immune response, or can prime the immune system of the mammalian host for anti-Leishmania immunity in response to a later infection.

In one embodiment, the immunogenic composition or the vaccine includes an effective amount of at least one *P. ariasi* polypeptide disclosed herein. The immunogenic composition and the vaccine can include a pharmaceutically acceptable excipient and/or an adjuvant. In one embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the composition includes a polypeptide having a sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:29, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:39, or SEQ ID NO:43, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, or SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, or SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a particular embodiment the immunogenic composition or vaccine comprises the five polypeptides as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, and SEQ ID NO:39. In a particular embodiment the immunogenic composition or vaccine comprises the four polypeptides as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, and SEQ ID NO:39.

In another embodiment, the immunogenic composition or the vaccine includes an effective amount of at least one *P. perniciosus* polypeptide disclosed

herein. The immunogenic composition or the vaccine can include a pharmaceutically acceptable excipient and/or an adjuvant. In one embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the immunogenic composition or vaccine includes a polypeptide having a sequence as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, or SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another embodiment, the immunogenic composition or vaccine includes a polypeptide having an amino acid sequence as set forth as SEQ ID NO:73, or SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a particular embodiment the immunogenic composition or vaccine comprises the four polypeptides as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, and SEQ ID NO:75. In another particular embodiment the immunogenic composition or vaccine comprises the two polypeptides as set forth as SEQ ID NO:73 and SEQ ID NO:75. In another particular embodiment the immunogenic composition or vaccine comprises the polypeptide as set forth as SEQ ID NO:75.

In a further embodiment, the immunogenic compositions and the vaccines may comprise a combination including at least one *P. ariasi* polypeptide disclosed herein and at least one *P. perniciosus* polypeptide disclosed herein. In one embodiment, the immunogenic composition or vaccine includes a combination of polypeptides including a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an

immunogenic fragment thereof, or any combination thereof. In another embodiment, the immunogenic composition or vaccine includes a combination of polypeptides including a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a
5 conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another
10 embodiment, the immunogenic composition or vaccine includes a combination of polypeptides including a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and a *P. perniciosus* polypeptide having an
15 amino acid sequence as set forth as SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another embodiment, the immunogenic composition or vaccine includes a combination of polypeptides including a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ
20 ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:75 a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a further embodiment, the immunogenic
25 composition or vaccine includes a combination of four *P. ariasi* polypeptides as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and two *P. perniciosus* polypeptides as set forth as SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a
30 homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the immunogenic composition or vaccine includes a combination of four *P. ariasi* polypeptides as set forth as SEQ ID NO:11, SEQ ID

NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and one *P. perniciosus* polypeptide as set forth as SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof.

In one embodiment, the immunogenic composition or the vaccine comprises an effective amount of a recombinant vector expressing at least one *P. ariasi* polypeptide disclosed herein and a pharmaceutically acceptable vehicle or excipient. In one specific, non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another specific, non-limiting example the recombinant vector encodes a polypeptide having a sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:29, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:39, or SEQ ID NO:43, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another specific, non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, or SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another specific, non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, or SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a particular embodiment the immunogenic composition or vaccine comprises recombinant vector(s) expressing at least the five polypeptides as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID

NO:35, and SEQ ID NO:39. In a particular embodiment the immunogenic composition or vaccine comprises recombinant vector(s) expressing at least the four polypeptides as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, and SEQ ID NO:39.

- 5 In another embodiment, the immunogenic composition or the vaccine comprises an effective amount of a recombinant vector expressing at least one *P. perniciosus* polypeptide disclosed herein and a pharmaceutically acceptable vehicle or excipient. In one specific, non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as set forth as SEQ ID NO:49, SEQ ID
- 10 NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another specific,
- 15 non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as set forth SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, or SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another specific, non-limiting example the recombinant vector encodes at least a polypeptide having a sequence as
- 20 set forth as SEQ ID NO:73, or SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a particular embodiment the immunogenic composition or vaccine comprises recombinant vector(s) expressing at least the four polypeptides as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, and SEQ ID NO:75. In a
- 25 particular embodiment the immunogenic composition or vaccine comprises recombinant vector(s) expressing at least the two polypeptides as set forth as SEQ ID NO:73, and SEQ ID NO:75. In a particular embodiment the immunogenic composition or vaccine comprises a recombinant vector expressing at least the polypeptide as set forth as SEQ ID NO:75.
- 30 In a further embodiment, the immunogenic composition or the vaccine comprises a combination including a recombinant vector encoding at least one *P. ariasi* polypeptide disclosed herein and encoding at least one *P. perniciosus*

polypeptide disclosed herein. In one embodiment, the combination includes a recombinant vector encoding at least a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, SEQ ID NO:75 a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the combination includes a recombinant vector encoding at least a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:55, SEQ ID NO:63, SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the combination includes a recombinant vector encoding at least a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In yet another embodiment, the combination includes a recombinant vector encoding at least a *P. ariasi* polypeptide having an amino acid sequence as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least a *P. perniciosus* polypeptide having an amino acid sequence as set forth as SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In a further embodiment, the combination includes recombinant vector(s) encoding at least four *P. ariasi* polypeptides as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID

NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least two *P. perniciosus* polypeptides as set forth as SEQ ID NO:73, SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof. In another embodiment, the combination includes recombinant vector(s) encoding at least four *P. ariasi* polypeptides as set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, SEQ ID NO:39, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and at least the *P. perniciosus* polypeptide as set forth as SEQ ID NO:75, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof.

In one embodiment, the *P. ariasi* polypeptide(s) having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, and the *P. perniciosus* polypeptide(s) having an amino acid sequence as set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, are encoded by the same recombinant vector. In another embodiment, the *P. ariasi* polypeptide(s) having an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, a conservative variant, a fusion protein, a homolog, or an

immunogenic fragment thereof, or any combination thereof, and the *P. perniciosus* polypeptide(s) having an amino acid sequence as set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, a conservative variant, a fusion protein, a homolog, or an immunogenic fragment thereof, or any combination thereof, are encoded by different recombinant vectors.

The *P. ariasi* polypeptide or a *P. perniciosus* polypeptide can be administered by any means known to one of skill in the art (See Banga, A., "Parenteral Controlled Delivery of Therapeutic Peptides and Proteins," *Therapeutic Peptides and Proteins*, Technomic Publishing Co., Inc., Lancaster, PA, 1995) such as by intramuscular, intradermal, subcutaneous, or intravenous injection, but even oral, nasal, or, anal administration is contemplated. In one embodiment, administration is by subcutaneous, intradermal, or intramuscular injection using a needleless injector (Biojector, Bioject, Oregon, USA).

To extend the time during which the peptide or protein is available to stimulate a response, the peptide or protein can be provided as an implant, an oily injection, or as a particulate system. The particulate system can be a microparticle, a microcapsule, a microsphere, a nanocapsule, or similar particle. (see, e.g., Banja, *supra*). A particulate carrier based on a synthetic polymer has been shown to act as an adjuvant to enhance the immune response, in addition to providing a controlled release. Aluminum salts may also be used as adjuvants to produce a humoral immune response. Thus, in one embodiment, a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide is administered in a manner to induce a humoral response.

In another embodiment, a *P. ariasi* polypeptide or a *P. perniciosus* polypeptide is administered in a manner to direct the immune response to a cellular response (that is, a CTL response), rather than a humoral (antibody) response. A number of means for inducing cellular responses, both *in vitro* and *in vivo*, are known. Lipids have been identified as agents capable of assisting in priming CTL *in vivo* against various antigens. For example, as described in U.S. Patent No. 5,662,907, palmitic acid residues can be attached to the alpha and epsilon amino

groups of a lysine residue and then linked (*e.g.*, via one or more linking residues, such as glycine, glycine-glycine, serine, serine-serine, or the like) to an immunogenic peptide. The lipidated peptide can then be injected directly in a micellar form, incorporated in a liposome, or emulsified in an adjuvant. As another
5 example, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinylserine can be used to prime tumor specific CTL when covalently attached to an appropriate peptide (*see*, Deres *et al.*, *Nature* 342:561, 1989). Further, as the induction of neutralizing antibodies can also be primed with the same molecule conjugated to a peptide which displays an appropriate epitope, the two compositions can be
10 combined to elicit both humoral and cell-mediated responses where that is deemed desirable.

In yet another embodiment, an MHC class II-restricted T-helper epitope is added to the polypeptide of the disclosure to induce T-helper cells to secrete cytokines in the microenvironment to activate CTL precursor cells. The technique
15 further involves adding short lipid molecules to retain the construct at the site of the injection for several days to localize the antigen at the site of the injection and enhance its proximity to dendritic cells or other "professional" antigen presenting cells over a period of time (*see* Chesnut *et al.*, "Design and Testing of Peptide-Based Cytotoxic T-Cell-Mediated Immunotherapeutics to Treat Infectious Diseases and
20 Cancer," Powell, *et al.*, (eds.), *Vaccine Design, the Subunit and Adjuvant Approach*, Plenum Press, New York, 1995).

An immunogenic composition or a vaccine according to the disclosure can be prepared in accordance with standard techniques well known to those skilled in the pharmaceutical or veterinary art. Such compositions can be administered in
25 dosages and by techniques well known to those skilled in the medical or veterinary arts, taking into consideration such factors as the age, sex, weight, species, and condition of the particular subject, and the route of administration. The immunogenic composition or the vaccine can be administered alone, or in combination with adjuvant(s) and/or with other antigen(s). The other antigen(s) can
30 be a *Leishmania* antigen. In one embodiment, the *Leishmania* antigen is the A2 antigen, such as the A2 antigen from *L. infantum* (*see* PCT Patent Application WO 95/06729 and in particular the sequence given in SEQ ID NO:2). The other

antigen(s) can be present in the composition as a protein, or as an immunological fragment thereof (*e.g.*, an epitope), or as an insert in an expression vector (*e.g.*, recombinant viral vector, recombinant plasmid, in particular the pVR1012 (Vical Inc.; Hartikka J. *et al.*, *Human Gene Therapy* 7:1205-1217, 1996)).

- 5 Any immunogenic composition, vaccine, or therapeutic composition according to the disclosure can be mixed with an adjuvant.

Polypeptide-based compositions:

- In several embodiments, the polypeptide-based immunogenic compositions and vaccines according to the disclosure are formulated with (1) vitamin E, saponin
10 (*e.g.*, Quil A™, QS21™), aluminum hydroxide, aluminum phosphate, aluminum oxide ("Vaccine Design, The subunit and adjuvant approach," *Pharmaceutical Biotechnology*, vol. 6, Edited by Micheal F. Powell and Mark J. Newman, 1995, Plenum Press New York), (2) an acrylic acid or methacrylic acid polymer, a polymer of maleic anhydride and of alkenyl derivative, (3) an immunostimulating sequence
15 (ISS), in particular an oligodeoxyribonucleotidic sequence bearing one or more non-methylated CpG groups (Klinman D. M. *et al.*, *Proc. Natl. Acad. Sci. USA* 93:2879-2883, 1996; WO 98/16247), (4) to formulate the immunogenic or vaccine preparation in the form of an oil-in-water emulsion, in particular the SPT emulsion described on page 147 of "Vaccine Design, The Subunit and Adjuvant Approach"
20 edited by M. Powell and M. Newman, Plenum Press, 1995, and the emulsion MF59 described on page 183 of this same book, (5) cytokines, or (6) combinations or mixtures thereof.

- The cytokine (5) could be added to the composition, such as, but not limited to, GM-CSF or cytokines inducing Th1 (*e.g.*, IL12). All these cytokines can be
25 added to the composition as a protein or as a vector encoding this cytokine protein. In one embodiment, the cytokines are from canine origin, *e.g.*, canine GM-CSF, for which a gene sequence has been deposited at the GenBank database (accession number S49738). This sequence can be used to create the vector in a manner similar to what was made in the PCT Patent Application WO 00/77210.

- 30 In one specific, non-limiting example the adjuvant contains two or more of an emulsifier, a micelle-forming agent, or an oil. Suitable emulsifiers, micelle-forming agents, and oils are detailed in U.S. Patent Nos. 5,585,103; 5,709,860;

5,270,202; and 5,695,770. An emulsifier is any molecule that allows the components of the emulsion to remain as a stable emulsion. Such emulsifiers include polysorbate 80 (Sorbitan-mono-9-octadecenoate-poly(oxy-1,2-ethanediyl); manufactured by ICI Americas, Wilmington, Del.), polysorbate 20, polysorbate 21, polysorbate 40, polysorbate 60, polysorbate 61, polysorbate 85, dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, TEEPOL HB7TM, and SPAN 80TM SPAN 85TM, ethoxylated fatty alcohols, ethoxylated fatty acids, ethoxylated castor oil (hydrogenated or not). In one embodiment, these emulsifiers are provided in an amount of approximately 0.05 to approximately 0.5%. In another embodiment, these emulsifiers are provided in an amount of approximately 0.2%. A micelle forming agent is an agent which is able to stabilize the emulsion formed with the other components such that a micelle-like structure is formed.

Examples of such agents include polymer surfactants described by BASF Wyandotte publications, *e.g.*, Schmolka, *J. Am. Oil. Chem. Soc.* **54**:110, 1977, and Hunter *et al.*, *J. Immunol.* **129**:1244, 1981, PLURONICTM L62LF, L101, L121, and L64, PEG1000, and TETRONICTM 1501, 150R1, 701, 901, 1301, and 130R1. The chemical structures of such agents are well known in the art. In one embodiment, the agent is chosen to have a hydrophile-lipophile balance (HLB) of between about 0 and about 2, as defined by Hunter and Bennett, *J. Immun.* **133**:3167, 1984. In one embodiment, the agent can be provided in an effective amount, for example between about 0.5 and about 10%. In another embodiment, the agent can be provided in an effective amount, for example between about 1.25 and about 5%.

In one embodiment, the oil included in the composition is chosen to promote the retention of the antigen in an oil-in-water emulsion, *i.e.*, to provide a vehicle for the desired antigen. In another embodiment, the oil has a melting temperature of less than about 65° C such that emulsion is formed either at room temperature (about 20° C to about 25° C), or once the temperature of the emulsion is brought down to room temperature.

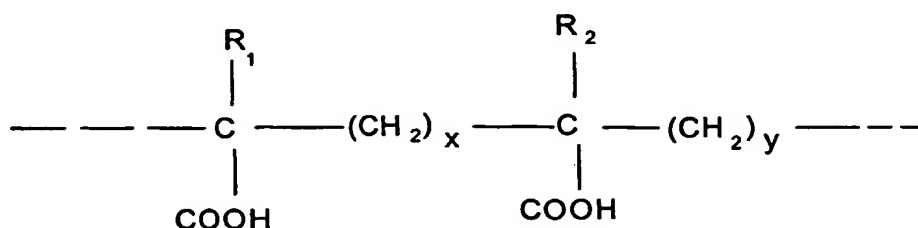
The oil-in-water emulsion (4) can be based in particular on light liquid paraffin oil (European Pharmacopea type); isoprenoid oil such as squalane, squalene, EICOSANETM or tetratetracontane; oil resulting from the oligomerization of alkenes, in particular of isobutene or decene; esters of acids or of alcohols

containing a linear alkyl group, more particularly plant oils, ethyl oleate, propylene glycol di(caprylate/caprate), glyceryl tri(caprylate/caprate) or propylene glycol dioleate; esters of branched fatty acids or alcohols, in particular isostearic acid esters. The oil is used in combination with emulsifiers to form the emulsion. In
5 several embodiments, the emulsifiers are nonionic surfactants, in particular esters of sorbitan, mannide (*e.g.*, anhydromannitol oleate), glycerol, polyglycerol, propylene glycol, and oleic, isostearic, ricinoleic, or hydroxystearic acid, which are for example, ethoxylated, and polyoxypropylene-polyoxyethylene copolymer blocks, in particular the Pluronic® products, especially L121. In one specific, non-limiting
10 example, the oil is provided in an amount between about 1 and about 60%. In another specific, non-limiting example, the oil is provided in an amount between about 5 and about 30%. In one embodiment, the adjuvant is a mixture of emulsifiers, micelle-forming agent, and oil available under the name Provax® (IDEC Pharmaceuticals, San Diego, CA).

15 The acrylic acid or methacrylic acid polymers (2) can be cross-linked in particular with polyalkenyl ethers of sugars or of polyalcohols. These compounds are known under the term "carbomer" (*Pharmeuropa*, Vol. 8, No. 2, June 1996). A person skilled in the art may also refer to U.S. Patent No. 2,909,462 describing such acrylic polymers cross-linked with a polyhydroxylated compound containing at least
20 3 hydroxyl groups. In one embodiment, a polyhydroxylated compound contains not more than 8 hydroxyl groups. In another embodiment, the hydrogen atoms of at least 3 hydroxyls are replaced with unsaturated aliphatic radicals containing at least 2 carbon atoms. In other embodiments, radicals contain from about 2 to about 4 carbon atoms, *e.g.*, vinyls, allyls, and other ethylenically unsaturated groups. The
25 unsaturated radicals can themselves contain other substituents, such as methyl. The products sold under the name Carbopol® (Noveon Inc., Ohio, USA) are particularly suitable. They are cross-linked with an allyl sucrose or with allylpentaerythritol. Among these, mention may be made of the products Carbopol® 974P, 934P, and 971P.

30 Among the copolymers of maleic anhydride and of an alkenyl derivative, such as the EMA® products (Monsanto) which are copolymers of maleic anhydride and of ethylene, which may be linear or cross-linked, for example cross-linked with

divinyl ether. Reference may be made to J. Fields *et al.*, *Nature* 186:778-780, 1960. In one embodiment, the acrylic acid or methacrylic acid polymers and the EMA® products are formed from units based on the following formula:



5

in which:

- R₁ and R₂, which may be identical or different, represent H or CH₃
- x = 0 or 1, in one embodiment, x = 1
- y = 1 or 2, with x + y = 2.

10 For the EMA® products, x = 0 and y = 2. For the carbomers, x = y = 1.

In one embodiment, the dissolution of these polymers in water leads to an acid solution, which is neutralized to physiological pH, in order to give the adjuvant solution into which the immunogenic composition or the vaccine itself is incorporated. The carboxyl groups of the polymer are then partly in COO⁻ form.

15 In one embodiment, a solution of adjuvant, especially of carbomer, is prepared in distilled water. In another embodiment, a solution of adjuvant, especially of carbomer, is prepared in the presence of sodium chloride, the solution obtained being at acidic pH. In another embodiment, this stock solution is diluted by adding it or a substantial part thereof, to the desired quantity (for obtaining the

20 desired final concentration) of water charged with NaCl. In yet another embodiment, stock solution is diluted by adding it to the desired quantity of physiological saline (NaCl 9 g/l) with concomitant or subsequent neutralization (pH 7.3 to 7.4). In one embodiment, the stock solution is neutralized with NaOH. This solution, at physiological pH, is used as is for mixing with the immunogenic

25 composition or with the vaccine, which may be stored in freeze-dried, liquid or frozen form.

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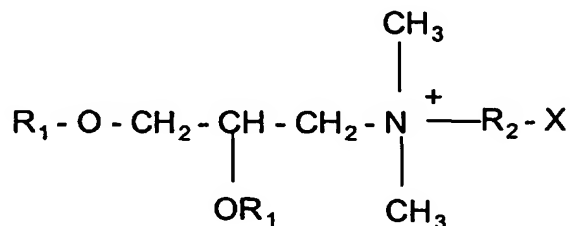
In one embodiment, the polymer concentration in the final vaccine composition is from about 0.01% to about 1.5% weight/volume (W/V). In another embodiment, the final vaccine composition is from about 0.05 to about 1% W/V. In yet another embodiment, the final vaccine composition is from about 0.1 to about 0.4% W/V.

Lipids have been identified as agents capable of stimulating the immune response for various antigens. For example, as described in U.S. Patent No. 5,662,907, palmitic acid residues can be attached to the alpha and epsilon amino groups of a lysine residue and then linked (e.g., via one or more linking residues, such as glycine, glycine-glycine, serine, serine-serine, or the like) to an immunogenic peptide. The lipidated peptide can then be injected directly in a micellar form, incorporated in a liposome, or emulsified in an adjuvant. As another example, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinylserine, can be used.

To extend the time during which the peptide or protein is available to stimulate a response, the peptide or protein can be provided as an implant, an oily injection, or as a particulate system. The particulate system can be a microparticle, a microcapsule, a microsphere, a nanocapsule, or similar particle. (see, e.g., Banja, *supra*). A particulate excipient based on a synthetic polymer has been shown to act as an adjuvant to enhance the immune response, in addition to providing a controlled release.

Plasmid-based compositions:

In one embodiment, the plasmid-based compositions is formulated with cationic lipids, in particular with cationic lipids containing a quaternary ammonium salt having the following formula:



in which R1 is a saturated or unsaturated linear aliphatic radical from 12 to 18 carbon atoms, R2 is another aliphatic radical comprising from 2 to 3 carbon atoms, and X is an hydroxyl or amine group.

In one embodiment, DMRIE (N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanammonium; WO 96/34109) is the cationic lipid. In another embodiment, the cationic lipid is in association with a neutral lipid, for example DOPE (dioleoyl-phosphatidyl-ethanolamine; Behr J. P., *Bioconjugate Chemistry* 5:382-389, 1994), in order to form the DMRIE-DOPE. In yet another embodiment, the mixture is made extemporaneously about 10 minutes to about 60 minutes before administration. In another embodiment, the mixture is made extemporaneously about 30 minutes before administration. In one embodiment, the molar ratio of DMRIE/DOPE is from about 95/5 to about 5/95. In another embodiment, the molar ratio of DMRIE/DOPE is about 1/1. In one embodiment, the weight ratio of plasmid/DMRIE or of DMRIE-DOPE adjuvant is from about 50/1 to about 1/10. In another embodiment, the weight ratio of plasmid/DMRIE or of DMRIE-DOPE adjuvant is from about 10/1 to about 1/5. In yet another embodiment, the weight ratio of plasmid/DMRIE or of DMRIE-DOPE adjuvant is from about 1/1 to about 1/2.

In one embodiment, a cytokine or non-methylated CpG groups is added to the composition, as described above for polypeptide-based compositions. The addition can be done advantageously by a plasmid encoding the cytokine.

Viral vector-based composition:

The recombinant viral vector-based composition can be supplemented with fMLP (N-formyl-methionyl-leucyl-phenylalanine; U.S. Patent No.: 6,017,537) and/or acrylic acid or methacrylic acid polymer adjuvant as described above for polypeptide-based compositions. They can also be formaluted with emulsions as described above.

In one embodiment, cytokines, non-methylated CpG groups, or emulsions are added to the composition as described above for polypeptide-based compositions. The addition can be done advantageously by a viral vector encoding said cytokine.

The immunogenic compositions and vaccines according to the disclosure are conserved and stored either in formulated form at 5°C, or in lyophilized form. In one embodiment, the immunogenic compositions and vaccines according to the disclosure are conserved and stored either in formulated form at 5°C, or in lyophilized form with a stabilizer. Freeze-drying can be done according to well-known standard freeze-drying procedures. The pharmaceutically acceptable stabilizers may be SPGA (sucrose phosphate glutamate albumin) (Bovarnik *et al.*, *J. Bacteriology* 59:509, 1950), carbohydrates (*e.g.*, sorbitol, mannitol, lactose, sucrose, glucose, dextran, trehalose), sodium glutamate (Tsvetkov T *et al.*, *Cryobiology* 20(3):318-23, 1983 ; Israeli E *et al.*, *Cryobiology* 30(5):519-23, 1993), proteins such as peptone, albumin, or casein, protein containing agents such as skimmed milk (Mills CK *et al.*, *Cryobiology* 25(2):148-52, 1988; Wolff E *et al.*, *Cryobiology* 27(5):569-75, 1990), and buffers (*e.g.*, phosphate buffer, alkaline metal phosphate buffer). An adjuvant may be used to make soluble the freeze-dried preparations.

15

Methods of Immunization

The present disclosure provides methods for inducing an immune response to a *Phlebotomus* polypeptide in a subject. The present disclosure provides further methods for inhibiting or preventing leishmaniasis in a subject.

20 These methods include the administration of at least one immunogenic composition or vaccine according to the disclosure.

 An immunogenic composition or a vaccine according to the disclosure can be prepared in accordance with standard techniques well known to those skilled in the pharmaceutical or veterinary art. Such compositions can be administered in dosages and by techniques well known to those skilled in the medical or veterinary arts, taking into consideration such factors as the age, sex, weight, species, and condition of the particular subject, and the route of administration.

25 If more than one administration is required, they can be administered concurrently (*e.g.*, different compositions given during the same period of time via the same or different routes, or a same composition given in the same period of time via different routes), or sequentially (*e.g.*, the same or different compositions given at least two times via the same or different routes). In one embodiment, the delay

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- between two sequential administrations is from about 1 week to about 6 months. In another embodiment, the delay is from about 3 weeks to about 6 weeks. In yet another embodiment, the delay is from about 4 weeks. Following vaccination, annual boost administrations may be done. In a prime-boost vaccination schedule
- 5 advantageously, at least one primo-administration can be done with a composition containing a plasmid according to the disclosure, following by at least one booster administration done with a composition containing a recombinant viral vector according to the disclosure, on the condition that a same *Phlebotomus* salivary polypeptide is present twice, coded by the plasmid and by the viral vector.
- 10 Alternatively, the booster administration can be done with a composition containing a polypeptide according to the disclosure, on the condition that a same *Phlebotomus* salivary polypeptide is present twice, coded by the primo-administration plasmid and in the booster polypeptide-based composition.

- In such compositions the antigen(s) may be in admixture with a suitable
- 15 vehicle or excipient such as sterile water, physiological saline, glucose, or the like. The compositions can contain auxiliary substances such as wetting or emulsifying agents, pH buffering agents, adjuvants, gelling, or viscosity enhancing additives, preservatives, flavoring agents, colors, and the like, depending upon the route of administration and the preparation desired. Standard texts, such as Remington's
- 20 *Pharmaceutical Science*, 17th edition, 1985, may be consulted to prepare suitable preparations, without undue experimentation. The compositions can also be lyophilized.

- Suitable dosages can also be based upon the examples below. For polypeptide-based compositions, the route of administration can be intradermal (ID),
- 25 intramuscular (IM), or subcutaneous (SC), intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector (Bioject, Oregon, USA). In several embodiments, polypeptide dosages can be from about 1 to 250 $\mu\text{g/ml}$, from about 15 to about 150 $\mu\text{g/dose}$, or from about 20 to about 100 $\mu\text{g/dose}$. In another
- 30 embodiment, using a needle-less apparatus, the volume of a dose can be between about 0.1 ml and about 0.5 ml. In yet another embodiment, using a needle-less apparatus, the volume of a dose can be about 0.25 ml. Administration with multiple

points of injection is preferred. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2 ml. In another embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.5 to about 1 ml.

- 5 For plasmid-based compositions, the route of administration can be ID, IM, SC, intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector. The dosage is from about 50 μ g to about 500 μ g per plasmid. When DMRIE-DOPE is added, about 100 μ g per plasmid is preferred. In one embodiment, when canine
- 10 GM-CSF or other cytokine is used, the plasmid encoding this protein is present at a dosage from about 200 μ g to about 500 μ g. In another embodiment, the plasmid encoding this protein is present at a dosage of about 200 μ g. In one embodiment, using a needle-less apparatus, the volume of a dose can be between about 0.1 ml and about 0.5 ml. In another embodiment, the volume of a dose can be about 0.25 ml.
- 15 In yet another embodiment, administration is performed using multiple points of injection. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2. In another embodiment, the volumes are from about 0.5 to about 1 ml. The dosages are the same as mentioned above.
- 20 For recombinant viral vector-based compositions, the route of administration can be ID, IM, SC, intravenous, oral, nasal, or anal. This administration can be made with a syringe and a needle or with a needle-less apparatus like, for example, Biojector. The dosage is from about 10^3 pfu to about 10^9 pfu per recombinant poxvirus vector. In one embodiment, when the vector is a canarypox virus, the
- 25 dosage is from about 10^5 pfu to about 10^9 pfu. In another embodiment, when the vector is a canarypox virus, the dosage is from about 10^6 pfu to about 10^8 pfu. In one embodiment, the volume of needle-less apparatus doses is between about 0.1 ml and about 0.5 ml. In another embodiment, the volume of needle-less apparatus dose is 0.25 ml. In yet another embodiment, administration is performed using multiple
- 30 points of injection. In one embodiment, for conventional injection with a syringe and a needle, the volumes are from about 0.1 to about 2. In another embodiment, the volumes are from about 0.5 to about 1 ml. The dosages are the same as

mentioned above. In one embodiment, when a syringe with a needle is used, the injection is IM.

In one embodiment, for the prime-boost administration regimen, the prime-administration is made with a plasmid-based composition and the boost
5 administration is made with a recombinant viral vector-based composition. In one embodiment, the boost administration is made with a canarypox vector. Both priming and boosting administrations include vectors encoding at least one identical *Phlebotomus* salivary antigen, and in one specific, non-limiting example, a *Leishmania* A2 antigen. The dosage of plasmids and recombinant viral vectors are
10 the same as described above. In one embodiment, the boost administration is done with a polypeptide-based composition. In specific, non-limiting examples, the dosage of polypeptide is from about 1 to about 250 µg/ml, from about 15 to about 150 µg/dose, or from about 20 to about 100 µg/dose.

Immunization by nucleic acid constructs is well known in the art and taught,
15 for example, in U.S. Patent No. 5,643,578 (which describes methods of immunizing vertebrates by introducing DNA encoding a desired antigen to elicit a cell-mediated or a humoral response) and U.S. Patent Nos. 5,593,972 and 5,817,637 (which describe operably linking a nucleic acid sequence encoding an antigen to regulatory sequences enabling expression). U.S. Patent No. 5,880,103 describes several
20 methods of delivery of nucleic acids encoding immunogenic peptides or other antigens to an organism. The methods include liposomal delivery of the nucleic acids (or of the synthetic peptides themselves), and immune-stimulating constructs, or ISCOMSTM, negatively charged cage-like structures of 30-40 nm in size formed spontaneously on mixing cholesterol and Quil ATM (saponin). Protective immunity
25 has been generated in a variety of experimental models of infection, including toxoplasmosis and Epstein-Barr virus-induced tumors, using ISCOMSTM as the delivery vehicle for antigens (Mowat and Donachie, *Immunol. Today* 12:383, 1991). Doses of antigen as low as 1 µg encapsulated in ISCOMSTM have been found to produce class I mediated CTL responses (Takahashi *et al.*, *Nature* 344:873, 1990).

30 In another approach to using nucleic acids for immunization, a *P. ariasi* or a *P. perniciosus* polypeptide, or an immunogenic peptide thereof, can also be expressed by attenuated viral hosts or vectors or bacterial vectors. Recombinant

vaccinia virus, adeno-associated virus (AAV), herpes virus, retrovirus, or other viral vectors can be used to express the peptide or protein, thereby eliciting a CTL response. For example, vaccinia vectors and methods useful in immunization protocols are described in U.S. Patent No. 4,722,848. BCG (Bacillus Calmette
5 Guerin) provides another vector for expression of the peptides (see Stover, *Nature* 351:456-460, 1991).

In one embodiment, a nucleic acid encoding a *P. ariasi* or a *P. perniciosus* polypeptide, or an immunogenic fragment thereof, is introduced directly into cells. For example, the nucleic acid may be loaded onto gold microspheres by standard
10 methods and introduced into the skin by a device such as Bio-Rad's Helios™ Gene Gun. A needless injector can also be utilized, such as a Bioinjector2000™. The nucleic acids can be "naked," consisting of plasmids under control of a strong promoter. Typically, the DNA is injected into muscle, although it can also be injected directly into other sites. Exemplary dosages for injection are around 0.5
15 µg/kg to about 50 mg/kg, and typically are about 0.005 mg/kg to about 5 mg/kg (see, e.g., U.S. Patent No. 5,589,466). In one embodiment, a prime-boost strategy for immunization is utilized. Thus, in one embodiment, a nucleic acid encoding a *P. ariasi* or a *P. perniciosus* polypeptide is administered to the subject, followed by immunization with an attenuated or inactivated form of *Leishmania*.

20 The immunogenic compositions and the vaccines disclosed herein can be administered for preventative and therapeutic treatments. In therapeutic applications, compositions are administered to a subject suffering from a disease, such as *Leishmaniasis*, in a therapeutically effective amount, which is an amount sufficient to cure or at least partially arrest the disease or a sign or symptom of the
25 disease. Amounts effective for this use will depend upon the severity of the disease and the general state of the subject's health. An effective amount of the compound is that which provides either subjective relief of a symptom(s) or an objectively identifiable improvement as noted by the clinician or other qualified observer.

Single or multiple administrations of the compositions are administered
30 depending on the dosage and frequency as required and tolerated by the subject. In one embodiment, the dosage is administered once as a bolus, but in another embodiment can be applied periodically until a therapeutic result is achieved.

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Generally, the dose is sufficient to treat or ameliorate symptoms or signs of disease without producing unacceptable toxicity in the subject.

As noted above, the dosage of the composition varies depending on the weight, age, sex, and method of administration. The dosage can also be adjusted by the individual physician as called for based on the particular circumstances. The compositions can be administered conventionally as vaccines containing the active composition as a predetermined quantity of active material calculated to produce the desired therapeutic or immunologic effect in association with the required pharmaceutically acceptable carrier or diluent (*i.e.*, carrier or vehicle). For example, about 50 µg of a DNA construct vaccine of the present disclosure can be injected intradermally three times at two week intervals to produce the desired therapeutic or immunologic effect. In another embodiment, about 1 mg/Kg dosage of a protein vaccine of the present disclosure can be injected intradermally three times at two week intervals to produce the desired therapeutic or immunologic effect.

A vaccine is provided herein that includes a *P. ariasi* or *P. perniciosus* polypeptide or polynucleotide. Administration of the vaccine to a subject, such as a human or veterinary subject, results in resistance to infection with *Leishmania*. In one embodiment, the subject is a human subject. In another embodiment, the subject is a canine subject, such as a dog.

The disclosure is illustrated by the following non-limiting Examples.

EXAMPLES

25

Example 1 Library Construction

Sand Flies and Preparation of salivary gland homogenate (SGH). Salivary extracts are prepared directly from sand flies captured in the wild in the Cevennes in Southern France (close to Vallerauge (Gard)) which is known to be a valid biotope for the *P. ariasi* sand fly species. Unfed females are captured by aspiration immediately after they land on the outside walls of a tent in which a dog has been placed. Captures are done at the end of July, shortly after dusk on dry days and in

the absence of wind. Outside temperatures should be between 20 and 25°C. Alternatively, salivary extracts of *P. perniciosus* are prepared directly from sand flies captured in the wild in Southern France (near the city of Marseille) which is known to be a valid biotope for the *P. perniciosus* sand fly species. The
5 identification of the sand fly specimen is performed by the visual observation (20x microscope) of the morphology of the spermatheca after dissection, as described in Leger *et al. Ann. Parasitol. Hum. Comp.* **158(6)**:611-623, 1983).

Salivary glands dissected under a dissection microscope and collected in microfuge tubes in sterile phosphate saline buffer, pH 7.0, are stored in dry ice and
10 transferred to -70 °C until use.

The salivary gland of *P. ariasi* is a sac-like structure consisting of a unicellular epithelium layer surrounding a large lumen (Adler and Theodor, *Ann. Trop. Med. Parasitol.* 20:109, 1926). After a blood meal, the gland total protein content decreases to half or less from its ~1µg value (Ribeiro *et al., Insect Biochem.*
15 19:409-412, 1989). Thus, most of the protein from the fly SGH must be destined for secretion. Sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) of SGH reveals a low complexity composition consisting of ~12 major bands varying from 10-100 kDa (Valenzuela *et al., J. Exp. Med.* 194:331-42, 2001). For
20 SDS-PAGE, Tris-glycine gels (16%), 1 mm thick, or NUPAGE 12% BIS-tris gels were used (Invitrogen). Gels were run with either Tris-glycine or MOPS Nupage running buffer according to the manufacturer's instructions. To estimate the molecular weight of the samples, See BlueJ markers from Invitrogen (myosin, BSA, glutamic dehydrogenase, alcohol dehydrogenase, carbonic anhydrase, myoglobin, lysozyme, aprotinin, and insulin, chain B) were used. SGH were treated with equal
25 parts of 2X SDS sample buffer (8% SDS in Tris-HCl buffer, 0.5M, pH 6.8, 10% glycerol and 1% bromophenol blue dye). Thirty pairs of homogenized salivary glands per lane (approximately 30µg protein) were applied when visualization of the protein bands by Coomassie blue staining was desired. For amino terminal sequencing of the salivary proteins, 40 homogenized pairs of glands were
30 electrophoresed and transferred to polyvinylidene difluoride (PVDF) membrane using 10 mM CAPS, pH 11, 10% methanol as the transfer buffer on a Blot-Module for the XCell II Mini-Cell (Invitrogen). The membrane was stained with Coomassie

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blue in the absence of acetic acid. Stained bands were cut from the PVDF membrane and subjected to Edman degradation using a Procise sequencer (Perkin-Elmer Corp.).

Salivary Gland cDNA Library Construction. *P. ariasi* salivary gland mRNA
5 was isolated from 100 salivary gland pairs from adult females. The
Micro-FastTrack mRNA isolation kit (Invitrogen, San Diego, CA) was used,
yielding approximately 100 ng poly (A)+ mRNA. The PCR-based cDNA library
was made following the instructions for the SMART cDNA library construction kit
(Clontech, Palo Alto, CA). One hundred nanograms of *P. ariasi* salivary gland
10 mRNA was reverse transcribed to cDNA using Superscript II RNase H- reverse
transcriptase (Gibco-BRL, Gaithersburg, MD) and the CDS/3' primer (Clontech,
Palo Alto, CA) for 1 hour at 42°C. Second strand synthesis was performed using a
PCR-based protocol by using the SMART III primer (Clontech, Palo Alto, CA) as
the sense primer, and the CDS/3' primer as anti-sense primer. These two primers,
15 additionally, create at the ends of the nascent cDNA, Sfi I A and B sites respectively.
Double strand cDNA synthesis was done on a Perkin Elmer 9700 Thermal cycler
(Perkin Elmer Corp., Foster City, CA) using the Advantage Klen-Taq DNA
polymerase (Clontech, Palo Alto, CA). PCR conditions were the following: 94° C
for 2 minutes; 19 cycles of 94° C for 10 seconds and 68° C for 6 minutes. Double
20 stranded cDNA was immediately treated with proteinase K (0.8 µg/µl) for 20
minutes at 45° C and washed three times with water using Amicon filters with a 100
kD cut off (Millipore Corp., Bedford MA). The double stranded cDNA was then
digested with Sfi I for 2 hours at 50° C (The Sfi I sites were inserted to the cDNA
during the second strand synthesis using the SMART III and the CDS/3' primer).
25 The cDNA was then fractionated using columns provided by the manufacturer
(Clontech, Palo Alto, CA). Fractions containing cDNA of more than 400 bp were
pooled, concentrated, and washed three times with water using an Amicon filter with
a 100 kDa cut-off. The cDNA was concentrated to a volume of 7 µl. The
concentrated cDNA was then ligated into a lambda triplex2 vector (Clontech, Palo
30 Alto, CA), and the resulting ligation reaction was packed using the Gigapack gold
III from Stratagene/Biocrest (Cedar Creek, TE) following manufacturer's
specifications. The obtained library was plated by infecting log phase XL1- blue

cells (Clontech, Palo Alto, CA) and the amount of recombinants was determined by PCR using vector primers flanking the inserted cDNA and visualized on a 1.1 % agarose gel with ethidium bromide (1.5 µg/ml)

Massive Sequencing of P. ariasi Salivary Gland cDNA Library. *P. ariasi* salivary gland cDNA library was plated to approximately 200 plaques per plate (150 mm Petri dish). The plaques were randomly picked and transferred to a 96 well polypropylene plate containing 100 µl of water per well. The plate was covered and placed on a gyrator shaker for 1 hour at room temperature. Four microliters of a phage sample was used as a template for a PCR reaction to amplify random cDNAs.

The primers used for this reaction were sequences from the triplex2 vector, the primers were named PT2F1 (5'- AAGTACTCT AGCAAT TGTGAGC- 3') (SEQ ID NO:85) which is positioned upstream of the cDNA of interest (5' end), and PT2R1 (5'- CTCTTCGCTATTACGCCAGCT G- 3') (SEQ ID NO:86) which is positioned downstream of the cDNA of interest (3' end). Platinum Taq polymerase (Gibco-BRL, Gaithersburg, MD) was used for these reactions. Amplification conditions were: 1 hold of 75° C for 3 minutes, 1 hold of 94° C for 3 minutes, and 34 cycles of 94° C for 30 seconds, 49° C for 30 seconds and 72° C for 1 minute and 20 seconds. Amplified products were visualized on a 1.1% agarose gel with ethidium bromide. Clean PCR was used as a template for a cycle sequencing reaction using the DTCS labeling kit from Beckman Coulter Inc. (Fullerton, CA). The primer used for sequencing (PT2F3) (5'- TCTCGGGAAGCGCGCCATTGTGTT - 3') (SEQ ID NO:87) is upstream of the inserted cDNA and downstream of the primer PT2F1. Sequencing reaction was performed on a Perkin Elmer 9700 thermacycler. Conditions were 75°C for 2 minutes, 94°C for 4 minutes, and 30 cycles of 96°C for 20 seconds, 50°C for 20 seconds and 60°C for 4 minutes.

After cycle sequencing the samples, a cleaning step was done using the multi-screen 96 well plate cleaning system from Millipore (Bedford, MA). The 96 well multi-screening plate was prepared by adding a fixed amount (according to the manufacturer's specifications) of Sephadex-50 (Amersham Pharmacia Biotech, Piscataway, NJ) and 300 µl of deionized water. After 1 hour of incubation at room temperature, the water was removed from the multi screen plate by centrifugation at

750 g for 5 minutes. After the Sephadex in the multi-screen plate was partially dried, the whole cycle sequencing reaction was added to the center of each well, centrifuged at 750 g for 5 minutes and the clean sample was collected on a sequencing microtiter plate (Beckman Coulter, Fullerton, CA). The plate was then
5 dried on Speed-Vac SC 110 model with a microtiter plate holder (Savant Instruments Inc, Holbrook, NY). The dried samples were immediately resuspended with 25 µl of deionized ultrapure formamide (J.T. Baker, Phillipsburg, NJ), and one drop of mineral oil was added to the top of each sample. Samples were sequenced immediately on a CEQ 2000 DNA sequencing instrument (Beckman Coulter Inc.,
10 Fullerton, CA) or stored at -30°C. The entire cDNA of selected genes was fully sequenced using custom primers using a CEQ 2000 DNA sequencing instrument (Beckman Coulter Inc., Fullerton, CA), as described above.

Accordingly, a cDNA library was also constructed with *P. perniciosus* salivary glands and sequenced.

15 *DNA Vaccine Construction and Description of the VR1020 Vector.* The genes coding for the predicted secreted proteins were amplified from *P. ariasi* specific cDNA and from *P. perniciosus* specific cDNA by PCR using Platinum *Taq* polymerase (GIBCO BRL) and specific primers carrying the Predicted N-terminus (Forward primer); and the stop codon (Reverse primer) of the selected cDNA.

20 The PCR product was immediately cloned into the custom made VR-2001-TOPO (derived from VR1020 vector) cloning vector following the manufacturer's specifications (Invitrogen). The ligation mixture was used to transform TOP10 cells (Invitrogen) and the cells were incubated overnight at 37° C. Eight colonies were picked and mixed with 10 µl of sterile water. Five µl of each sample were
25 transferred to Luria broth (LB) with ampicillin (100 µg/ml) and grown at 37° C. The other 5 µl were used as a template for a PCR reaction using two vector-specific primers from the PCRII vector to confirm the presence of the insert and for sequencing analysis. After visualization of the PCR product on a 1.1% agarose gel, the eight PCR products were completely sequenced as described above using a
30 CEQ2000 DNA sequencing instrument (Beckman Coulter). Cells containing the plasmid carrying the selected *P. ariasi* gene were grown overnight at 37° C on Luria broth with ampicillin (100 µg/ml), and plasmid isolation was performed using the

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Wizard Miniprep kit (Promega). The VR-2001-TOPO (a variant of the VR1020 plasmid from Vical) plasmid contains a kanamycin resistance gene, the human cytomegalovirus promoter, and the tissue plasminogen activator signal peptide upstream of the TOPO TA cloning site. The sample that contained the sequence
 5 from the start codon to the stop codon in the right orientation and in the correct open-reading-frame following the nucleotide sequence encoding the tissue plasminogen activator signal peptide was chosen.

Plasmids were transformed into the SCS-1 strain of *E. coli* (Stratagene, La Jolla, CA) according to the manufacturer's instructions. The transformed bacteria
 10 were grown in LB medium and the plasmid was subsequently purified using a commercial plasmid purification kit (Qiagen, Courtaboeuf, France). Individual plasmids were quality controlled for identity based on a restriction profile.

15 These plasmids were named and encoded the following proteins:

Table 1

Plasmid name	Protein encoded
PJV001	PRL-P4-A10
PJV002	PRL-P4-D6
PJV003	PRL-P4-E5
PJV004	PRL-P4-G7
PJV005	PRM-P5-D6
PJV006	PRM-P5-E9
PJV007	PRM-P5-F12
PJV008	PRM-P5-F2
PJV009	PRM-P5-G11
PJV010	PRM-P5-H4
PJV011	PRS-P1-B11
PJV012	PRS-P1-B4
PJV013	PRS-P1-E7
PJV014	PRS-P1-G9
PJV015	PRS-P2-C8
PJV016	PRS-P2-G8
PJV017	PRL-P4-A9
PJV018	PRL-P4-C10
PJV019	PRL-P4-D7
PJV020	PRL-P4-F3
PJV021	PRL-P4-G12

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PJV022	PRL-P6-E11
PJV023	PRM-P3-A6
PJV024	PRM-P3-F11
PJV031	PERL-P7-G8
PJV032	PERL-P6-H9
PJV033	PERL-P7-C2
PJV034	PERL-P6-H1
PJV035	PERL-P3-E11
PJV036	PERL-P7-G12
PJV037	PERL-P3-C9
PJV038	PERM-P2-A10
PJV039	PERL-P6-H11
PJV040	PERS-P1-H11
PJV041	PERM-P2-G11
PJV042	PERM-P5-E2
PJV025	PERM-P5-C11
PJV026	PERM-P5-H8
PJV027	PERL-P3-B3
PJV028	PERM-P2-D11
PJV029	PERM-P5-E3
PJV030	PERM-P2-F11

Example 2

DNA and Predicted Protein Sequence Analysis.

- 5 DNA data derived from the mass sequencing project were analyzed by an in-house program written in VisualBASIC (Microsoft). This program removed vector and primer sequences from the raw sequence. Stripped sequences were compared to the NCBI non-redundant protein database using the program BlastX using the BLOSUM-62 matrix (Altschul *et al. Nucleic Acids Research* 25:3389, 1997). DNA
- 10 sequences were clustered by blasting the database against itself with a preselected threshold cutoff, usually $1e^{-10}$ (BlastN program) (Altschul *et al. Nucleic Acids Research* 25:3389, 1997). Sequences from the same cluster were aligned using ClustalX (Jeanmougin *et al., Trends Biochem. Sci.* 23:403, 1998). To find the cDNA sequences corresponding to the amino acid sequence obtained by Edman
- 15 degradation of the proteins transferred to PVDF membranes from SDS-PAGE gels, a search program was written that checked these amino acid sequences against the three possible protein translations of each cDNA sequence obtained in the mass

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sequencing project. This was written using the same approach used in the BLOCKS (Henikoff *et al.*, *Bioinformatics* 15:471, 1999) or Prosite (Bairoch, *Nucleic Acids Res.* 19(Suppl.):2241,1991) programs. Protein translations of the full-length clones were further processed to identify the predicted signal peptides using the Signal P
5 program (Nielsen *et al.*, *Protein Eng.* 10:1, 1997), available online. Predicted signal peptide cleaved sites were compared to the N-terminus sequence obtained from Edman degradation of *Phlebotomus* salivary proteins. Estimation of isoelectric point and molecular weight of translated protein was performed using the DNA STAR program (DNASTAR). Full-length translated protein sequence information
10 was compared with the non-redundant protein database of NCBI using the BLAST-P program (Altschul *et al.* *Nucleic Acids Research* 25:3389, 1997) and searched for motifs by submitting each sequence to the electronic database.

To characterize the primary structure of the main proteins of *P. ariasi* and *P. perniciosus* SGH, SDS-PAGE gels were transferred to PVDF membranes, and the
15 amino terminal sequence of each cut band by Edman degradation was estimated.

Example 3

DNA Vaccination in Mice

For genetic immunization, Swiss Webster mice were purchased from
20 Taconic Farms. Mice were maintained in the NIAID Animal Care Facility under pathogen-free conditions. Mice were inoculated in the right ear with 30 µg of the plasmid encoding the selected cDNA from *P. ariasi* suspended in 5 µl of PBS. Each group was boosted 2 wk later using the same regimen. Mice were challenged on the opposite ear with salivary gland homogenate of *P. ariasi* and delayed type
25 hypersensitivity (DTH) response was measured 24 hours after the injection by measuring thickness and redness of ear (++: at least 2 mice with a good DTH response, +++ : at least three mice had a good DTH response, Table 2).

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Table 2

Plasmid name	DTH response
PJV002	-
PJV016	-
PJV008	-
PJV017	-
PJV021	+++
PJV013	-
PJV024	+++
PJV022	+++
PJV007	-
PJV005	+++
PJV009	+++
PJV023	++
PJV010	-
PJV012	+++
PJV003	-
PJV014	-
PJV015	++
PJV019	-
PJV018	-
PJV011	-
PJV020	+++
PJV001	+++
PJV006	+++
PJV004	++

5

Example 4**Production of an Immune Response in Dogs**

In a first experiment DTH (delayed type hypersensitivity) reaction was performed in dogs with natural immunity against the leishmaniasis in order to determine which *P. ariasi* salivary proteins are recognized by a protective immune response. Dogs with natural immunity survived without symptoms after two years of exposure in an endemic area. In a second experiment, naïve dogs were immunized with the 24 *P. ariasi* salivary gland proteins expressed by a plasmid in order to evaluate the capability to induce a cellular immune response measured by DTH.

Twelve dogs approximately three years old with natural immunity against Leishmaniasis were injected, via an intradermal route (ID) in the back after shaving, with 100µg of each individual plasmid suspended in 100µl of PBS. Each plasmid

was injected at a different point. The points were separated by at least 3 cm to avoid interference between DTH responses. The negative control (100 μ l of buffer) was also inoculated by ID route.

- 5 The DTH response was assessed 72 hours after injection by measuring the larger diameter of the skin tumefaction area (see Table 3). The results are expressed as the mean value of the tumefaction area for all the dogs and as a percentage of dogs having a positive DTH response. A positive DTH is a tumefaction area diameter greater than or equal to 4 mm at 72 hours after injection.

Table 3

10

Plasmids	Mean diameter of the tumefaction area (mm)	Percentage of dogs with a tumefaction diameter \geq 4mm
PJV018	1.1	18%
PJV016	1.4	20%
PJV005	2.0	27%
PJV006	1.4	27%
PJV008	2.0	27%
PJV011	1.6	27%
PJV013	1.7	27%
PJV020	1.4	27%
PJV023	1.5	27%
PJV015	2.4	36%
PJV024	2.1	36%
PJV004	2.3	40%
PJV009	2.9	46%
PJV014	2.7	46%
PJV019	2.9	46%
PJV002	2.8	46%
PJV021	3.3	55%
PJV007	3.3	55%
PJV017	3.9	58%
PJV001	4.4	64%
PJV022	4.1	64%
PJV003	6.0	82%
PJV012	6.1	91%
PJV010	6.3	100%

The data in Table 3 can be divided into three groups: a first group corresponding to plasmids number PJV001, PJV022, PJV003, PJV012, and PJV010 showing a strong DTH response, a second group corresponding to PJV018, PJV016, PJV005, PJV006, PJV008, PJV011, PJV013, PJV020, PJV023, PJV015, and PJV024 showing a low DTH response, and a last group (with PJV004, PJV009, PJV014, PJV019, PJV002, PJV021, PJV007, and PJV017) showing an intermediate DTH response.

In a second study, 10 naïve dogs 4 to 6 months old were immunized by ID injection in 10 points (100µl per point) in the right ear with a pool of the 24 plasmids (PJV001 to PJV024), 100µg for each one suspended in 1000µl of PBS. On day 21, dogs were injected in 10 points (100µl per point) in the left ear and in 10 points (100µl per point) in the belly with a pool of the 24 plasmids, 100µg for each one suspended in 2000µl of PBS. All dogs were challenged on day 35 by inoculation by ID route in the back (after shaving), with 100µg of each individual plasmid suspended in 100µl of PBS. Each plasmid was injected at a different point. The points were separated by at least 3 cm to avoid interference. As a negative control, 100µl of buffer was inoculated intradermally. The DTH response was assessed 72 hours after challenge, by measuring the larger diameter of the skin tumefaction area (see Table 4). The results are expressed as the mean value of the tumefaction area for all the dogs and as a percentage of dogs having a positive DTH response. A positive DTH is a tumefaction area diameter higher or equal of 4 mm at 72 hours after injection.

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Table 4

Plasmids	Mean diameter of the tumefaction area (mm)	Percentage of dogs with a tumefaction diameter ≥ 4 mm
PJV018	4.2	60%
PJV016	3.2	56%
PJV005	3.9	60%
PJV006	3.3	50%
PJV008	3.9	70%
PJV011	4.9	89%
PJV013	3.2	56%
PJV020	2.5	50%
PJV023	3.9	67%
PJV015	2.7	44%
PJV024	5.3	78%
PJV004	3.8	56%
PJV009	3.7	70%
PJV014	2.9	44%
PJV019	1.8	33%
PJV002	2.7	50%
PJV021	4.2	70%
PJV007	3.5	70%
PJV017	3.1	56%
PJV001	2.1	40%
PJV022	6.4	100%
PJV003	4.3	70%
PJV012	3.2	60%
PJV010	2.4	40%

The results of this table show that all plasmids can induce cellular immunity in dogs
5 after injection, as revealed by a DTH response. The variation of the DTH response
level may be due to the variation of the expression of the insert.

It will be apparent that the precise details of the methods described may be
varied or modified without departing from the spirit of the described disclosure. We
10 claim all such modifications and variations that fall within the scope and spirit of
the claims below.

CLAIMS

We claim:

- 5 1. A substantially purified salivary *P. ariasi* polypeptide.
2. The polypeptide of claim 1, wherein the polypeptide comprises
- a) an amino acid sequence at least 80% identical to a the amino acid
sequence set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7,
10 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17,
SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27,
SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37,
SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID
NO:47,
- 15 b) a conservative variant of the amino acid sequence set forth as SEQ ID
NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11,
SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21,
SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31,
SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41,
20 SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47
- c) an immunogenic fragment comprising eight consecutive amino acids of
the amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5,
SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15,
SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25,
25 SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35,
SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45,
or SEQ ID NO:47, that specifically binds to an antibody that specifically binds the
amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ
ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID
30 NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID
NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID

NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, respectively; or

- d) the amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, wherein administration of the polypeptide to a subject produces an immune response to *P. ariasi*.

10

3. The *P. ariasi* polypeptide of claim 2, wherein the polypeptide comprises an amino acid sequence as set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47, or a conservative variant thereof.

4. The *P. ariasi* polypeptide of claim 3, wherein the polypeptide comprises an amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47.

25

5. An antigenic fragment of the polypeptide of claim 4.

6. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO:11, SEQ ID NO:19, SEQ ID NO:35, or SEQ ID NO:39.

30

7. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:33, SEQ ID NO:39, or SEQ ID NO: 45.

8. An isolated nucleic acid encoding the polypeptide of claim 1.

9. The nucleic acid of claim 8, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48, or a degenerate variant thereof.

10. The nucleic acid of claim 8, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, or SEQ ID NO:48.

11. The nucleic acid of claim 8, wherein the nucleic acid encodes an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:12, SEQ ID NO: 20, SEQ ID NO:36, or SEQ ID NO: 40.

12. The nucleic acid of claim 8, wherein the nucleic acid encodes an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:2, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID

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NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:34, SEQ ID NO:40, or SEQ ID NO: 46.

13. The nucleic acid of claim 8, operably linked to an expression control
5 sequence.

14. The nucleic acid of claim 13, wherein the expression control sequence
comprises a promoter.

10 15. The nucleic acid of claim 14, wherein the promoter comprises an
inducible or constitutive promoter.

16. The nucleic acid of claim 15, wherein the promoter comprises a
cytomegalovirus promoter.

15

17. A vector comprising the nucleic acid of claim 8.

18. The vector of claim 17, wherein the vector comprises a plasmid.

20 19. The vector of claim 17, wherein the vector comprises a viral vector.

20. A host cell transformed with the vector of claim 17.

21. An antibody that specifically binds the polypeptide of claim 1.
25

22. The antibody of claim 21, wherein the antibody comprises a monoclonal
antibody.

23. The antibody of claim 21, comprising a detectable label.
30

24. The antibody of claim 23, wherein the label comprises a fluorescent,
enzymatic or radioactive label.

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25. A pharmaceutical composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier.

5 26. A pharmaceutical composition comprising the nucleic acid of claim 8 and a pharmaceutically acceptable carrier.

10 27. A method for inducing an immune response to a *P. ariasi* polypeptide in a subject, comprising
 administering to the subject a therapeutically effective amount of the *P. ariasi* polypeptide of claim 1, or a polynucleotide encoding the polypeptide the *P. ariasi* polypeptide of claim 1, thereby inducing the immune response.

15 28. The method of claim 27, wherein the immune response comprises a T cell response.

 29. The method of claim 27, wherein the immune response comprises a B cell response.

20 30. The method of claim 27, wherein the subject comprises a non-human veterinary subject.

 31. The method of claim 27, wherein the subject is a dog.

25 32. The method of claim 23, wherein the subject is a human.

 33. The method of claim 27, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:11, SEQ ID NO: 19, SEQ ID NO:35, or SEQ ID NO: 39.

30 34. The method of claim 27, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ

ID NO:1, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:33, SEQ ID NO:39, or SEQ ID NO: 45.

- 5 35. A method for inhibiting a symptom of a *Leishmania* infection or preventing a *Leishmania* infection in a subject, comprising administering to the subject a therapeutically effective amount of the *P. ariasi* polypeptide of claim 1, or a polynucleotide encoding the polypeptide, thereby inhibiting the symptom of the *Leishmania* infection or preventing the *Leishmania* infection.

10

36. The method of claim 35, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:11, SEQ ID NO: 19, SEQ ID NO:35, or SEQ ID NO: 39.

- 15 37. The method of claim 35, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:1, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:33, SEQ ID NO:39, or SEQ ID NO: 45.

20

38. Use of a composition comprising the polypeptide of claim 1 or a nucleic acid encoding the polypeptide of claim 1 for the manufacture of a medicament.

39. A substantially purified salivary *P. perniciosus* polypeptide.

25

40. The polypeptide of claim 39, wherein the polypeptide comprises
a) an amino acid sequence at least 80% identical to a the amino acid
sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID
NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID
30 NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID
NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83;

b) a conservative variant of the amino acid sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83;

c) an immunogenic fragment comprising eight consecutive amino acids of the amino acid sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, that specifically binds to an antibody that specifically binds the amino acid sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, respectively; or

d) the amino acid sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, wherein administration of the polypeptide to a subject produces an immune response to *P. perniciosus*.

41. The *P. perniciosus* polypeptide of claim 40, wherein the polypeptide comprises an amino acid sequence as set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83, or a conservative variant thereof.

30

42. The *P. perniciosus* polypeptide of claim 41, wherein the polypeptide comprises an amino acid sequence set forth as SEQ ID NO:49, SEQ ID NO:51, SEQ

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ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, or SEQ ID NO:83.

5

43. An antigenic fragment of the polypeptide of claim 42.

44. The polypeptide of claim 39, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:55, SEQ ID NO: 63, SEQ ID NO:73, or SEQ ID NO: 75.

10

45. The polypeptide of claim 39, wherein the polypeptide comprises an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO:73 or SEQ ID NO: 75.

15

46. An isolated nucleic acid encoding the polypeptide of claim 39.

47. The nucleic acid of claim 46, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84, or a degenerate variant thereof.

20

48. The nucleic acid of claim 46, wherein the nucleic acid comprises a sequence as set forth as SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, or SEQ ID NO:84.

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49. The nucleic acid of claim 46, wherein the nucleic acid encodes an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:56, SEQ ID NO: 64, SEQ ID NO:74, or SEQ ID NO:76.

5 50. The nucleic acid of claim 46, wherein the nucleic acid encodes an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:74 or SEQ ID NO: 76.

10 51. The nucleic acid of claim 46, operably linked to an expression control sequence.

52. The nucleic acid of claim 51, wherein the expression control sequence comprises a promoter.

15 53. The nucleic acid of claim 52, wherein the promoter comprises an inducible or constitutive promoter.

20 54. The nucleic acid of claim 52, wherein the promoter comprises a cytomegalovirus promoter.

55. A vector comprising the nucleic acid of claim 46.

56. The vector of claim 55, wherein the vector comprises a plasmid.

25 57. The vector of claim 55, wherein the vector comprises a viral vector.

58. A host cell transformed with the vector of claim 55.

30 59. An antibody that specifically binds the polypeptide of claim 39.

60. The antibody of claim 59, wherein the antibody comprises a monoclonal antibody.

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61. The antibody of claim 59, comprising a detectable label.

62. The antibody of claim 61, wherein the label comprises a fluorescent,
5 enzymatic, or radioactive label.

63. A pharmaceutical composition comprising the polypeptide of claim 39
and a pharmaceutically acceptable carrier.

10 64. A pharmaceutical composition comprising the nucleic acid of claim 46
and a pharmaceutically acceptable carrier.

65. A method for inducing an immune response to a *P. perniciosus*
polypeptide in a subject, comprising
15 administering to the subject a therapeutically effective amount of the *P.*
perniciosus polypeptide of claim 39, or a polynucleotide encoding the polypeptide
the *P. perniciosus* polypeptide of claim 39, thereby inducing the immune response.

66. The method of claim 65, wherein the immune response comprises a T
20 cell response.

67. The method of claim 65, wherein the immune response comprises a B
cell response.

25 68. The method of claim 65, wherein the subject comprises a non-human
veterinary subject.

69. The method of claim 65, wherein the subject is a dog.

30 70. The method of claim 65, wherein the subject is a human.

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71. The method of claim 65, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:55, SEQ ID NO: 63, SEQ ID NO:73, or SEQ ID NO: 75.

5 72. The method of claim 65, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:73 or SEQ ID NO: 75.

10 73. A method for inhibiting a symptom of *Leishmania* or preventing *Leishmania* infection in a subject comprising administering to the subject a therapeutically effective amount of the *P. perniciosus* polypeptide of claim 39, or a polynucleotide encoding the polypeptide, thereby inhibiting the symptom of *Leishmania* or preventing the *Leishmania* infection.

15 74. The method of claim 73, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:55, SEQ ID NO: 63, SEQ ID NO:73, or SEQ ID NO: 75.

20 75. The method of claim 73, wherein the polypeptide comprises an amino acid sequence at least 80% identical to a the amino acid sequence set forth as SEQ ID NO:73 or SEQ ID NO: 75.

25 76. Use of a composition comprising the polypeptide of claim 39 or a nucleic acid encoding the polypeptide of claim 39 for the manufacture of a medicament.

SEQUENCE LISTING

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REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND
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Valenzuela, Jesus G.
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Belkaid, Yasmine
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METHODS OF USE

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tgctatcata gcttatgacc tgactaagga caattatcct gagattgacg gatacgagat      480
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gattgtgtac gatcaggaga agaaagattc ttggaagatc agtcatgggt catttaaacc      660
cgaacatgag tcgattctaa tccataacgg ggttgatcat attttaaaac tgggtatttt      720
cggaatcacc cttggagatc gggattcgga gggaaaccgt ccggcttact acttaggagg      780
aagcagtacg aagctctttg aagtcaacac aaaggctctt aagaagaagg agggtgaaat      840
cgaaccaatc actctgggag atcgtggacc tcattccgaa gccattgctt tggcatacga      900
tcccaagacc aaagtgattt tcttactga atataactct aagaagatct catgctggaa      960
catcaagaaa ccccttattc atgacaacat ggataagatt tatgctagtc ctgaatttat     1020
tttcggcact gatatttcgg ttgatagtg atccaaattg tggttcttct ccaacggaca     1080
tccaccatt gagaatctgc agttgagctc tgataagcct catattcatc ttataagcgt     1140
ggatacggaa aaggcaattc gtggcactaa atgtgaagtg aaggcctaag tcaaaaatat     1200
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aaaaaaaaa                                     1268

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<210> 7

<211> 393

<212> PRT

<213> *Phlebotomus ariasi*

<400> 7

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Met Lys Ile Phe Met Gly Leu Ile Ala Val Val Ser Leu Gln Gly Ala
1           5           10           15

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Leu Ala Tyr His Val Glu Arg Glu Tyr Ala Trp Lys Asn Ile Thr Phe
 20 25 30

Glu Gly Ile Asp Gln Ala Ser Tyr Asn Ile Glu Asn Ser Ile Pro Thr
 35 40 45

Ala Phe Val His Asp Ala Leu Ser Lys Lys Ile Ile Ile Ala Ile Pro
 50 55 60

Arg Leu Tyr Pro Gln Val Pro Ile Thr Leu Thr Gln Leu Asp Thr Thr
 65 70 75 80

Lys His Pro Glu Arg Ser Pro Pro Leu Glu Lys Phe Pro Gly Ser Asp
 85 90 95

Lys Leu Thr Ser Val Tyr Gln Pro Met Leu Asp Glu Cys Arg Arg Leu
 100 105 110

Trp Ile Val Asp Val Gly Gln Val Glu Tyr Lys Gly Asp Glu Gln Lys
 115 120 125

Tyr Pro Lys Lys Asn Pro Ala Ile Ile Ala Tyr Asp Leu Thr Lys Asp
 130 135 140

Asn Tyr Pro Glu Ile Asp Arg Tyr Glu Ile Pro Ile Asn Ile Ala Gly
 145 150 155 160

Asn Gln Ile Gly Phe Gly Gly Phe Thr Val Asp Val Thr Asn Pro Lys
 165 170 175

Glu Gly Cys Gly Lys Thr Phe Ile Tyr Ile Thr Asn Phe Glu Asp Asn
 180 185 190

Thr Leu Ile Val Tyr Asp Gln Glu Lys Lys Asp Ser Trp Lys Ile Ser
 195 200 205

His Gly Ser Phe Lys Pro Glu His Glu Ser Asn Phe Ser His Asn Gly
 210 215 220

Ala Gln Tyr Lys Tyr Lys Ala Gly Ile Phe Gly Ile Thr Leu Gly Asp
 225 230 235 240

Arg Asp Pro Glu Gly Asn Arg Pro Ala Tyr Tyr Leu Gly Gly Ser Ser
 245 250 255

Thr Lys Leu Phe Glu Val Ser Thr Glu Ala Leu Lys Lys Lys Gly Ala
260 265 270

Lys Phe Asp Pro Val Arg Leu Gly Asp Arg Gly Arg His Thr Glu Ala
275 280 285

Ile Ala Leu Val Tyr Asp Pro Lys Thr Lys Val Ile Phe Phe Ala Glu
290 295 300

Ser Asp Ser Arg Gln Ile Ser Cys Trp Asn Thr Gln Lys Pro Leu Asn
305 310 315 320

His Lys Asn Thr Asp Val Ile Tyr Ala Ser Ser Lys Phe Ile Phe Gly
325 330 335

Thr Asp Ile Gln Ile Asp Ser Asp Ser Gln Leu Trp Phe Leu Ser Asn
340 345 350

Gly Gln Pro Pro Ile Asp Asn Leu Lys Leu Thr Phe Asp Lys Pro His
355 360 365

Ile Arg Leu Met Arg Val Asp Thr Lys Asn Ser Ile Arg Arg Thr Arg
370 375 380

Cys Glu Val Lys Pro Ile Lys Lys Pro
385 390

<210> 8
<211> 1306
<212> DNA
<213> Phlebotomus ariasi

<400> 8
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atagatcaag catcctacaa cattgaaaac agcatcccaa ctgcattcgt tcacgatgca 180
cttagtaaga agattatcat cgctattcct aggetatata ctcaggtgcc aattacttta 240
actcaacttg ataccaccaa gcatccggaa cgttctctc ctctcgaaaa attccctgga 300
agcgataaat taacctctgt ttatcaaccg atgcttgacg aatgtcgtag actttggatt 360
gttgacgttg gacaggtcga gtacaaggga gatgagcaga agtaccctaa gaaaaatcct 420
gctatcatag cctatgacct gactaaggac aattatccag agattgatcg atatgagata 480
ccgattaata ttgctggtaa tcaaatagga tttggaggat ttaccgttga tgttacgaat 540

ccgaaggagg gatgtggttaa aacctttatc tacatcacga acttcgaaga caacactctg 600
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 gaacatgagt ctaatttctc ccacaacggt gctcagtaca agtacaaagc gggatatttc 720
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 cccccattg ataatctcaa attgactttt gataagcccc atattcgtct tatgagggta 1140
 gatacgaaaa attcaattcg taggactaga tgtgaagtga agcccatcaa gaagccataa 1200
 gacaatctat taaaaatgta acaatttccc caaaaaaaga aattgtaaat ttacgatga 1260
 taataaaaaa attttatgct tgtgaaaaaa aaaaaaaaaa aaaaaa 1306

<211> 292

<212> PRT

<213> Phlebotomus ariasi

<400> 9

Met Phe Lys Glu Ile Ile Val Val Ala Leu Ala Val Ile Val Ala Gln
 1 5 10 15

Cys Ala Pro Pro Ala Ile Pro Ile Ala Lys Gln Gly Asn Asp Phe Pro
 20 25 30

Val Pro Ile Val Asp Glu Lys Glu Thr Asp Asp Phe Phe Asp Asp Arg
 35 40 45

Phe Tyr Pro Asp Ile Asp Asp Glu Arg Val Gly Ala Arg Ala Pro Val
 50 55 60

Gly Gly Lys Gln Thr Ser Asn Arg Gly Thr Ser Ser Gln Ser Asp Lys
 65 70 75 80

Val Pro Arg Pro Gln Gly Ser Asn Arg Gly Pro Ser Ser Gln Thr Thr
 85 90 95

Asp Lys Val Pro Arg Pro Gln Trp Pro Ser Arg Gly Thr Asn Ser Gln
 100 105 110

Asn Asp Lys Val Pro Arg Pro Gln Gly Ser Ser Gly Gln Thr Pro Pro
 115 120 125

Arg Thr Pro Gly Lys Val Glu Gln Ser Gly Arg Thr Asn Thr Lys Asp
 130 135 140

Gln Ile Pro Arg Pro Leu Thr Asn Arg Asn Pro Thr Lys Asn Pro Thr
 145 150 155 160

Glu Gln Ala Arg Arg Pro Gly Asn Arg Glu Leu Leu Ile Arg Asp Lys
 165 170 175

Thr Pro Gly Ser Gln Gly Gly Lys Gln Gly Thr Gly Asn Arg Gln Lys
 180 185 190

Leu Ser Ser Tyr Lys Asp Ala Gln Pro Lys Leu Ile Phe Lys Ser Ser
 195 200 205

Gln Phe Asn Thr Asp Gly Gln Asn Pro Tyr Leu Thr Arg Leu Phe Lys
 210 215 220

Thr Lys Lys Val Glu Glu Val Ile Ala Lys Gly Ser Pro Thr Asp Glu
 225 230 235 240

Tyr Val Leu Glu Leu Leu Asp Gly Lys Pro Asp Asn Leu Ser Leu Val
 245 250 255

Ile Arg Thr Asn Gly Lys Thr Ser Gln Ala Val Leu Arg Asn Pro Thr
 260 265 270

Arg Asn Arg Ile Val Gly Arg Ile Lys Ser Tyr Asn Pro Gly Pro Arg
 275 280 285

Arg Met Ser Tyr
 290

<210> 10
 <211> 992
 <212> DNA
 <213> Phlebotomus ariasi

<400> 10
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 cccaattgtt gatgaaaagg aaacggatga tttctttgac gatcgattct atccggacat 180

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agatgatgag cgtgtaggtg ctagggctcc ggtgggtggc aaacagacat ctaatagagg      240
aaccagttct cagagtgata aggttcctcg tcctcaaggg tccaatagag ggcctagctc      300
tcagactact gacaagggtc cccgtcctca atggcccagt agaggaacca attctcagaa      360
tgacaagggt cctcgtcctc aagggtctag tggacaaact ccacctagaa cgcctggaaa      420
ggttgaacaa agtgggaagga ccaacacaaa ggaccaaata cctcgtccac tgactaacag      480
aaacccaacc aagaacccaa ctgaacaggc tagaagacca ggaaacaggg agctactcat      540
tagggataaa accccagggg gtcaagggtg aaaacaggga acaggcaata ggcagaaact      600
gtcgagttat aaagacgctc agccgaagtt gattttcaaa tcgagtcaat tcaatactga      660
tggccaaaat ccatatttaa cgaggttggt caagacgaag aaagtcgaag aagttatagc      720
taaaggaagt cccactgatg aatatgtcct ggagcttttg gatggaaagc cagataatct      780
gagcttggtc atcagaacaa atggcaagac gagccaagcg gttctcagga atcccactcg      840
caacagaatt gtgggccgta tcaagtcgta caaccccggc ccgaggcgaa tgtcctatta      900
atTTTTTTTT ctctTTTTtc tcctaaatac aactcccaca ataaaatttc agttgtacgc      960
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<210> 11
<211> 312
<212> PRT
<213> Phlebotomus ariasi

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<400> 11

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Met Ala Ser Ile Lys Leu Ser Thr Cys Ser Phe Val Leu Leu Asn Leu
1           5           10          15

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```

Ile Leu Pro Thr Ile Ser Met Lys Val Ile Ser Phe Asp Asp Arg Asp
20           25          30

```

```

Glu Tyr Leu Leu Gly Lys Pro Ala Asn Ser Asp Asp Glu Leu Leu Tyr
35           40          45

```

```

Ser Thr Phe Asp Phe Gln Arg Asp Pro Cys Ser Lys Ser Tyr Val Lys
50           55          60

```

```

Cys Thr Asn Asn Asn Thr His Phe Ile Leu Asp Phe Val Asp Pro Lys
65           70          75          80

```

```

Lys Arg Cys Ile Ser Ser Ile His Val Phe Ser Tyr Pro Asp Arg Pro
85           90          95

```

Pro Ser Phe Glu Glu Lys Arg Ile Pro Ser Lys Ser Ala Ile Tyr Cys
 100 105 110

Gln Lys Gly Gly Ile Gly Lys Ser His Cys Leu Leu Val Phe Arg Lys
 115 120 125

Lys Glu Pro Arg Glu Asp Ala Leu Val Asp Ile Arg Gly Ile Pro Ala
 130 135 140

Asp Gln Thr Cys Ser Leu Lys Glu Arg Tyr Thr Ser Gly Asp Pro Lys
 145 150 155 160

Lys Thr Asp Ala Tyr Gly Met Ala Tyr Gln Phe Asp Arg Lys Asp Asp
 165 170 175

Trp His Ile Gln Arg Thr Gly Ile Lys Thr Trp Lys Arg Ser Gly Asn
 180 185 190

Glu Ile Phe Tyr Arg Lys Asn Gly Leu Met Asn His Gln Ile Arg Tyr
 195 200 205

Leu Ser Lys Phe Asp Lys Tyr Thr Val Thr Arg Glu Leu Val Val Lys
 210 215 220

Asn Asn Ala Lys Lys Phe Thr Leu Glu Phe Ser Asn Phe Arg Gln Tyr
 225 230 235 240

Arg Ile Ser Phe Leu Asp Ile Tyr Trp Phe Gln Glu Ser Gln Arg Asn
 245 250 255

Lys Pro Arg Leu Pro Tyr Ile Tyr Tyr Asn Gly His Cys Leu Pro Ser
 260 265 270

Asn Lys Thr Cys Gln Leu Val Phe Asp Thr Asp Glu Pro Ile Thr Tyr
 275 280 285

Ala Phe Val Lys Val Phe Ser Asn Pro Asp His Asn Glu Pro Arg Leu
 290 295 300

Arg His Glu Asp Leu Gly Arg Gly
 305 310

<210> 12
 <211> 1047
 <212> DNA

<213> Phlebotomus ariasi

<400> 12

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gagtatctac ttggtaaacc tgcaaattct gacgatgaac ttctctattc aacctttgac      180
ttccagagag atccctgttc taagtcttac gtgaagtga ccaacaacaa caccacttt      240
attctggatt tcgttgatcc gaagaagaga tgcattctct caattcacgt tttctcctac      300
cccgatagac ctcccagctt tgaggagaag aggattccct cgaagagtgc aatttactgc      360
caaaagggcg gcattgggaa gagtcactgt ttgctggtgt tcaggaagaa ggaacctcga      420
gaggacgcac tggttgatat ccggggaatc cccgctgac aaacatgctc cctcaaggag      480
cgctacacat cgggagatcc taagaaaacc gatgcttacg gaatggccta tcagtttgat      540
agaaaagatg attggcacat tcaaagaaca ggtatcaaga catggaaaag atcaggaaac      600
gagatcttct accgtaagaa tggtttaatg aaccatcaaa taaggtactt gagcaagttc      660
gacaaataca cggttaccag agaattggtg gtgaagaaca acgctaagaa attcaccttg      720
gaattttcaa acttcctgca ataccgaatc agtttcttgg acatctactg gttccaggag      780
tctcagagga ataaaccag attaccttat atttactaca acggtcattg cttgcctagc      840
aacaagacat gccagttggt cttcgacact gatgagccta ttacttatgc ttttgtgaaa      900
gtgttttagta atccggatca caatgaacca cgactaagac atgaagatct aggacgaggg      960
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<210> 13

<211> 375

<212> PRT

<213> Phlebotomus ariasi

<400> 13

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Met Val Ile Tyr Leu Thr Gln Asn Ile Ser Arg Ala Leu Leu Thr Leu
1           5           10           15

```

```

Leu Pro Asn Pro Glu Asp Val Arg Ser Ala Ala Asp Val Leu Glu Ser
20           25           30

```

```

Phe Thr Asp Asp Leu Lys Ser Phe Tyr Pro Pro Pro Asp Asp Val Asn
35           40           45

```

```

Glu Glu Val Ser Glu Thr Glu Ser Arg Thr Lys Arg Ser Leu Ile Glu
50           55           60

```

Gln Leu Lys Glu Ser Gln Pro Leu Lys Gln Ile Arg Glu Thr Val Ala
65 70 75 80

Glu Thr Thr Lys Tyr Leu Lys Gly Phe Leu Lys Thr Lys Pro Ser Gly
85 90 95

Asn Gln Thr Glu Ser Ser Asn Ser Thr Ser Thr Lys Thr Gln Ser Arg
100 105 110

Lys Arg Arg Gly Leu Thr Asp Phe Ile Pro Val Asn Ser Leu Lys Asp
115 120 125

Ala Ile Ser Gln Ala Thr Ser Gly Ala Met Lys Ala Phe Lys Pro Ser
130 135 140

Ser Glu Asn Lys Thr Ser Ser Asn Pro Leu Asp Phe Leu Ala Ser Leu
145 150 155 160

Ser Asp Ile Ser Arg Asp Leu Val Gln Asn Ser Ile Lys Glu Val Ser
165 170 175

Gly Asn Leu Val Ser Ser Val Ala Leu Tyr Gln Val Asn Ser Lys Leu
180 185 190

Asp Ala Ile Lys Gln Ser Ile Gly Ile Ile Asn Gln Glu Ile Asp Arg
195 200 205

Thr Lys Lys Val Gln Gln Tyr Val Met Asn Ala Leu Gln Gln Ala Ser
210 215 220

Asn Ile Thr Asn Ser Ile Gly Glu Gln Leu Lys Ser Asn Asn Cys Phe
225 230 235 240

Ala Gln Phe Ile Asn Pro Phe Lys Leu Phe Glu Glu Val Ile Thr Cys
245 250 255

Val Lys Asn Lys Ile Glu Asn Gly Leu Lys Ile Ala Glu Glu Thr Phe
260 265 270

Lys Asn Leu Asn Gln Ala Leu Ser Val Pro Ser Asp Ile Val Ser Glu
275 280 285

Val Ser Lys Cys Ser Gln Asn Gln Asn Leu Asn Pro Leu Thr Lys Leu
290 295 300

Leu Cys Tyr Leu Arg Val Pro Leu Gln Leu Asp Glu Glu Lys Leu Leu
305 310 315 320

Leu Pro Ile Glu Phe Ala Arg Arg Ile Arg Glu Ile Thr Asn Tyr Phe
325 330 335

Ala Thr Met Arg Met Asp Leu Ile Gln Cys Gly Ile Ala Thr Ile Gln
340 345 350

Ser Ile Gly Asp Lys Val Glu Asn Cys Ala Ile Glu Ala Ile Leu Ala
355 360 365

Val Lys Asp Thr Leu Lys Gly
370 375

<210> 14
<211> 1263
<212> DNA
<213> Phlebotomus ariasi

<400> 14

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cagagtcaag	aactaagaga	tcattgattg	agcaactcaa	agagtcgcaa	cctctaaaac	240
aaatcagaga	aacagttgct	gagacaacca	agtagctaaa	gggattctta	aaaacgaaac	300
cttctggaaa	tcaaacggag	agttctaact	caacaagtac	gaagactcag	tcaagaaaga	360
gacgtggatt	aactgatttt	ataccagtga	attctctaaa	ggatgcaatt	tcacaagcaa	420
cttcaggtgc	catgaaagcg	ttcaaaccct	caagtgaaaa	taaaacaagt	tcaaadcctc	480
tagatttcct	cgcaagcctc	tcagatattt	ccagagatct	tgtacaaaat	tcaattaagg	540
aagtctctgg	caatttagtt	tcaagcgttg	ctttatacca	agtcaactca	aagttagatg	600
ccattaaaca	atccattggg	atcataaatc	aagaaattga	taggaccaa	aaagttcagc	660
aatacgtcat	gaatgctctt	caacaagcca	gcaatattac	taactcaatt	ggagagcaac	720
tcaagtccaa	caactgtttc	gcacaattta	taaaccatt	caaacttttc	gaagaagtaa	780
taacttggtg	gaaaaataaa	atcgaaaatg	gattgaaaat	tgcggaagag	acatttataa	840
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aaaaccagaa	cttgaatccc	ttgacgaaac	ttctgtgcta	cttgagggtg	cccctgcaat	960
tggatgagga	gaaactgctg	cttcctattg	aatttgcgag	gcgaattaga	gaaataacca	1020

actatatttgc caccatgaga atggacctca ttcaatgtgg catagcaact attcaatcaa 1080
 tcggagacaa gggttgagaat tgtgcaatag aagcaatatt ggctgtaaaag gacactttga 1140
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 attgtgtatg tatattgaga aaatgaataa atgcttcaaa atgaaaaaaaa aaaaaaaaaa 1260
 aaa 1263

<210> 15
 <211> 138
 <212> PRT
 <213> Phlebotomus ariasi

<400> 15

Met Lys Gln Phe Pro Val Ile Leu Leu Thr Leu Gly Leu Leu Val Val
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Lys Cys Arg Ser Glu Arg Pro Glu Trp Lys Cys Glu Arg Asp Phe Lys
 20 25 30

Lys Ile Asp Gln Asn Cys Phe Arg Pro Cys Thr Phe Ala Ile Tyr His
 35 40 45

Phe Val Asp Asn Lys Phe Arg Ile Ala Arg Lys Asn Ile Glu Asn Tyr
 50 55 60

Lys Lys Phe Leu Ile Asp Tyr Asn Thr Val Lys Pro Glu Val Asn Asp
 65 70 75 80

Leu Glu Lys His Leu Leu Asp Cys Trp Asn Thr Ile Lys Ser Ile Glu
 85 90 95

Ala Ser Ser Arg Thr Glu Lys Cys Glu Gln Val Asn Asn Phe Glu Arg
 100 105 110

Cys Val Ile Asp Lys Asn Ile Leu Asn Tyr Pro Val Tyr Phe Asn Ala
 115 120 125

Leu Lys Lys Ile Asn Lys Asn Thr Asn Val
 130 135

<210> 16
 <211> 530
 <212> DNA
 <213> Phlebotomus ariasi

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<400> 16
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atcgacaaaa attgctttcg tccttgatca tttgcaattt accactttgt tgataacaag      180
ttcaggattg ccaggaagaa tattgaaaac tacaagaagt tcttaattga ctataacacc      240
gtgaagcccc aagttaatga tttggaaaaa cacctgttag attgttgga tacaatcaaa      300
tccattgaag catcatccag gacggaaaaa tgtgaacaag ttaacaactt tgaacgatgt      360
gttattgaca agaacattct taattatcct gtttacttca atgctttgaa gaaaataaat      420
aagaatacaa atgtttaatt aaataaagat gtgaaatatt gcagtgacaa aatataaaaa      480
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      530

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<210> 17
<211> 388
<212> PRT
<213> Phlebotomus ariasi

```

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<400> 17

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Met Ile Asn Pro Ile Val Leu Arg Phe Thr Phe Leu Leu Val Ile Leu
1           5           10          15

```

```

Leu Pro Gly Lys Cys Lys Ser Ala Pro Lys Ser Cys Thr Ile Asn Leu
          20          25          30

```

```

Pro Thr Ser Ile Pro Lys Lys Gly Glu Pro Ile Tyr Leu Asn Ser Asn
          35          40          45

```

```

Gly Ser Val Phe Arg Pro Ile Gly Gly Leu Thr Gln Leu Asn Ile Gly
          50          55          60

```

```

Asp Ser Leu Ser Ile Tyr Cys Pro Pro Leu Lys Lys Leu Lys Ser Val
65           70           75          80

```

```

Pro Cys Ser Arg Lys Phe Ser Leu Glu Ser Tyr Ser Cys Asn Asn Ser
          85          90          95

```

```

Ser Gln Ser Glu Leu Val Gln Thr Glu Glu Glu Cys Gly Gln Glu Gly
          100         105         110

```

```

Lys Trp Tyr Asn Ile Gly Phe Pro Leu Pro Thr Asn Ala Phe His Thr
          115         120         125

```

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Ile Tyr Arg Thr Cys Phe Asn Lys Gln Lys Leu Thr Pro Ile Tyr Ser
          19

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130 135 140

Tyr His Val Ile Asn Gly Lys Ala Val Gly Tyr His Val Lys Gln Pro
145 150 155 160

Arg Gly Asn Phe Arg Pro Gly Lys Gly Val Tyr Arg Lys Ile Asn Ile
165 170 175

Asn Glu Leu Tyr Lys Thr His Ile Ser Arg Phe Lys Lys Val Phe Gly
180 185 190

Asp Lys Gln Thr Phe Phe Arg Lys Pro Leu His Tyr Leu Ala Arg Gly
195 200 205

His Leu Ser Pro Glu Val Asp Phe Val Phe Gly Thr Glu Gln His Ala
210 215 220

Thr Glu Phe Tyr Ile Asn Thr Ala Pro Gln Tyr Gln Ser Ile Asn Gln
225 230 235 240

Gly Asn Trp Leu Arg Val Glu Lys His Val Arg Gly Leu Ala Lys Ala
245 250 255

Leu Gln Asp Asn Leu Leu Val Val Thr Gly Ile Leu Asp Ile Leu Lys
260 265 270

Phe Ser Asn Lys Arg Ala Asp Thr Glu Ile Tyr Leu Gly Asp Gly Ile
275 280 285

Ile Pro Val Pro Gln Ile Phe Trp Lys Ala Ile Phe His Leu Arg Thr
290 295 300

Ser Ser Ala Ile Val Phe Val Thr Ser Asn Asn Pro His Glu Thr Thr
305 310 315 320

Phe Asn Asn Ile Cys Lys Asp Ala Cys Glu Met Ala Gly Phe Gly Asp
325 330 335

Lys Gln His Gly Asn Gln Asn Phe Ser Asn Tyr Ser Leu Gly Phe Thr
340 345 350

Ile Cys Cys Glu Leu Gln Asp Phe Ile Gly Asn Ser Lys Val Val Leu
355 360 365

Pro Lys Asp Ile Gln Val Lys Asn His Arg Lys Leu Leu Gln Leu Pro
20

370

375

380

Lys Pro Lys Gln
385

<210> 18
<211> 1268
<212> DNA
<213> *Phlebotomus ariasi*

<400> 18
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ccaccagcat tccaagaaa ggtgaaccga ttacctcaa cagtaatgga tcagttttcc 180
gacctattgg aggtttaact caactcaaca ttggggactc cctctccatc tactgtccac 240
cactgaagaa gctcaagagt gttccttgca gtcgaaaatt ctcccttgag agctactctt 300
gcaacaacag ctctcagagt gaactcgtgc agacggagga ggagtgcgga caagagggga 360
aatggtacaa cattggcttt ccattgcccc caaatgcctt ccacacaatc tacagaactt 420
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acaacagac attcttccgg aagccactgc actacctggc tcgcgacat ctctccctg 660
aagtggactt tgtcttcggc accgaacaac acgccactga gttctacatc aacaccgccc 720
cccagtatca gtccatcaac cagggaaatt ggctgcgagt tgaaaaacac gtgcgcggtc 780
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<210> 19
<211> 252

<212> PRT

<213> Phlebotomus ariasi

<400> 19

Met Asn Ala Leu Leu Leu Cys Val Leu Leu Ser Leu Ser Gly Ile Gly
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20 25 30

Arg Thr Cys Gln Arg Glu Gly Lys Asp Pro Ala Leu Val Ser Lys Trp
35 40 45

Met Asn Trp Val Leu Pro Asp Asp Pro Glu Thr His Cys Tyr Val Lys
50 55 60

Cys Val Trp Thr Asn Leu Gly Ser Tyr Asp Asp Asn Thr Gly Ser Ile
65 70 75 80

Met Ile Asn Thr Val Ala Thr Gln Phe Ile Thr Arg Gly Met Lys Val
85 90 95

Pro Ala Glu Val Asn Asn Leu Ser Gly Ser Thr Ser Gly Ser Cys Ser
100 105 110

Asp Ile Tyr Lys Lys Thr Ile Gly Phe Phe Lys Ser Gln Lys Ala Asn
115 120 125

Ile Gln Lys Ala Tyr Tyr Gly Thr Lys Glu Glu Ser Asp Asn Trp Tyr
130 135 140

Ser Lys His Pro Asn Val Lys Pro Lys Gly Thr Lys Ile Ser Asp Phe
145 150 155 160

Cys Lys Gly Arg Glu Gly Gly Thr Glu Gly Thr Tyr Lys His Ala Cys
165 170 175

Ser Met Tyr Tyr Tyr Arg Leu Val Asp Glu Asp Asn Leu Val Ile Pro
180 185 190

Phe Arg Lys Leu Lys Ile Pro Gly Ile Pro Gly Pro Lys Ile Asp Glu
195 200 205

Cys Arg Arg Lys Ala Ser Ser Lys Thr Gly Cys Lys Val Ala Asp Ala
210 215 220

Leu Tyr Lys Cys Leu Lys Ala Ile Asn Gly Lys Ser Phe Glu Asn Ala
 225 230 235 240

Leu Lys Lys Leu Asp Glu Glu Ser Ser Arg Thr Tyr
 245 250

<210> 20

<211> 838

<212> DNA

<213> Phlebotomus ariasi

<400> 20

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<210> 21

<211> 113

<212> PRT

<213> Phlebotomus ariasi

<400> 21

Met Ile Arg Ile Leu Phe Pro Leu Phe Ile Leu Ser Leu Gly Ile Tyr
 1 5 10 15

Gln Val Thr Cys Leu Met Cys His Ser Cys Thr Leu Asp Gly Glu Leu
 20 25 30

Glu Ser Cys Glu Asp Ser Ile Asn Glu Thr Tyr Val Val Lys Ile Glu
 23

35

40

45

Glu Lys Glu Cys Lys Pro Ala Gln Ser Cys Gly Lys Val Ser Phe Thr
50 55 60

Ala Asn Gly Thr Val Arg Ile Gly Arg Gly Cys Ile Arg Ser Ser Ser
65 70 75 80

Ser Trp Lys Ile Asp Cys Arg Ile Leu Ala Lys Glu Val Arg Asp Glu
85 90 95

Gly Ile Ala Val Thr His Cys Ser Leu Cys Asp Thr Asp Leu Cys Asn
100 105 110

Glu

<210> 22
<211> 492
<212> DNA
<213> Phlebotomus ariasi

<400> 22
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aaaaaaaaaa aa 492

<210> 23
<211> 277
<212> PRT
<213> Phlebotomus ariasi

<400> 23

Met Leu Gln Ile Lys His Phe Leu Phe Phe Val Val Leu Phe Val Val
1 5 10 15

Ala His Ser Asn Asp Tyr Cys Glu Pro Lys Leu Cys Lys Phe Asn Asn

24

20

25

30

Gln Val Lys Thr His Ile Gly Cys Lys Asn Asp Gly Lys Phe Val Glu
35 40 45

Ser Thr Cys Pro Lys Pro Asn Asp Ala Gln Met Ile Asp Met Thr Glu
50 55 60

Gln Arg Lys Asn Leu Phe Leu Lys Ile His Asn Arg Leu Arg Asp Arg
65 70 75 80

Leu Ala Arg Gly Ser Val Ser Asn Phe Lys Ser Ala Ala Lys Met Pro
85 90 95

Met Leu Lys Trp Asp Asn Glu Leu Ala Arg Leu Ala Glu Tyr Asn Val
100 105 110

Arg Thr Cys Lys Phe Ala His Asp Gln Cys Arg Ser Thr Lys Ala Cys
115 120 125

Pro Tyr Ala Gly Gln Asn Leu Gly Gln Met Leu Ser Ser Pro Asp Phe
130 135 140

Leu Asp Pro Asn Tyr Val Ile Lys Asn Ile Thr Arg Glu Trp Phe Leu
145 150 155 160

Glu Tyr Lys Trp Ala Asn Gln Gly His Thr Asp Lys Tyr Met Thr Gly
165 170 175

Ser Gly Lys Asn Gly Lys Ala Ile Gly His Phe Thr Ala Phe Ile His
180 185 190

Glu Lys Ser Asp Lys Val Gly Cys Ala Val Ala Lys Leu Thr Asn Gln
195 200 205

Gln Tyr Asn Met Lys Gln Tyr Leu Val Ala Cys Asn Tyr Cys Tyr Thr
210 215 220

Asn Met Leu Lys Glu Gly Ile Tyr Thr Thr Gly Lys Pro Cys Ser Gln
225 230 235 240

Cys Gln Gly Lys Lys Cys Asp Ser Val Tyr Lys Asn Leu Cys Asp Ala
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Ser Glu Lys Val Asp Pro Ile Pro Asp Ile Phe Lys Gln Ser Arg Gln

260

265

270

Gln Arg Ser Arg Lys
275

<210> 24
<211> 1067
<212> DNA
<213> Phlebotomus ariasi

<400> 24
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<210> 25
<211> 249
<212> PRT
<213> Phlebotomus ariasi

<400> 25

Met Ile Val Lys Ser Phe Leu Gly Val Phe Leu Val Ile Leu Leu Val
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Ser Val Thr Glu Gln Asp Arg Gly Val Asp Gly His Arg Arg Thr Gln
 20 25 30

Asp Asp His Asp Tyr Ser Glu Leu Ala Glu Tyr Asp Asp Glu Asp Pro
 35 40 45

His Gln Glu Val Ile Asp Gly Asp Glu Glu Glu His Glu Leu Ser Gly
 50 55 60

Gly Arg Arg Leu Ser His Glu Asp Glu Asp Asp Asp Arg His Tyr
 65 70 75 80

Gly His Arg Gly Glu Asp Arg Glu Asn Ser Arg Gly Arg Asn Gly Gly
 85 90 95

Ser Arg Asn Arg Gly Ser Glu Glu Gln Ser Tyr Asp Pro Tyr Ser His
 100 105 110

Glu Arg Ala Pro Thr Tyr Ser Glu Ser Ser Glu Tyr Asp His Ser Gly
 115 120 125

Asp Tyr Asp Asn Ser Asn Tyr Gln Gln His Ser Ser Thr Pro Ser Ser
 130 135 140

Tyr Ser Asn Ile Asp His Tyr Leu His Leu Ile Gln Leu His Ser Val
 145 150 155 160

Pro Ser Asp Leu Ala Gln Tyr Ala Asp Ser Tyr Leu Gln His Ser Lys
 165 170 175

Asn Ser Ile Arg Tyr Tyr Ala Ser His Ala Lys Asp Phe Glu Lys Ile
 180 185 190

Arg Pro Cys Leu Glu Ser Val Val Lys Tyr Ser Asn Leu Leu Asn Asp
 195 200 205

Asp Leu Ala Lys Glu Tyr Ile Arg Cys Gln Arg Lys Cys Tyr Leu Glu
 210 215 220

Arg Leu Asn Ser Tyr Thr Ser Ala Ile Ser Gln Tyr Thr Val Thr Thr
 225 230 235 240

Asn Ala Cys Ile Asn Asn Arg Leu His
 245

<210> 26
 <211> 914
 <212> DNA
 <213> Phlebotomus ariasi

<400> 26
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<210> 27
 <211> 333
 <212> PRT
 <213> Phlebotomus ariasi

<400> 27

Met Ile Ile Lys Leu Cys Ala Ile Ala Val Ala Cys Leu Leu Thr Gly
 1 5 10 15

Asp Gly Glu Ala Ala Pro Arg Ala Thr Arg Phe Ile Pro Phe Ala Val
 20 25 30

Ile Ser Asp Leu Asp Lys Lys Ser Ile Lys Ser Asp Gln Lys Ser Phe
 35 40 45

Thr Ser Ile Val Arg Tyr Gly Glu Leu Lys Asp Asn Gly Glu Arg Tyr
 28

50	55	60
Thr Leu Ser Ile Lys Ser Glu Asn Leu His Tyr Phe Thr Arg Tyr Ala 65 70 75 80		
Tyr Asn Gly Arg Gly Ala Glu Leu Ser Glu Leu Leu Tyr Phe Asn Asn 85 90 95		
Lys Leu Tyr Thr Ile Asp Asp Lys Thr Gly Ile Ile Phe Glu Val Lys 100 105 110		
His Gly Gly Asp Leu Ile Pro Trp Val Ile Leu Ser Asn Gly Asp Gly 115 120 125		
Asn Gln Lys Asn Gly Phe Lys Ala Glu Trp Ala Thr Val Lys Gly Asp 130 135 140		
Lys Leu Ile Val Gly Ser Thr Gly Ile Pro Trp Phe Glu Glu Lys Thr 145 150 155 160		
Gln Ser Leu Asn Thr Tyr Ser Leu Trp Val Lys Glu Ile Ser Lys Glu 165 170 175		
Gly Glu Val Thr Asn Ile Asn Trp Lys Ser Gln Tyr Ser Lys Val Lys 180 185 190		
Asn Ala Met Gly Ile Pro Ser Ser Val Gly Phe Val Trp His Glu Ala 195 200 205		
Val Asn Trp Ser Pro Arg Lys Asn Leu Trp Val Phe Met Pro Arg Lys 210 215 220		
Cys Thr Thr Glu Tyr Phe Thr Ser Gln Val Glu Glu Lys Thr Gly Cys 225 230 235 240		
Asn Gln Ile Ile Thr Ala Asn Glu Asp Phe Thr Gln Val Lys Ala Ile 245 250 255		
Arg Ile Asp Gly Pro Val Gln Asp Gln Ala Ala Gly Phe Ser Ser Phe 260 265 270		
Lys Phe Ile Pro Gly Thr Gln Asn Asn Asp Ile Phe Ala Leu Lys Thr 275 280 285		
Ile Glu Arg Asn Gly Gln Thr Ala Thr Tyr Gly Thr Val Ile Asn Ile		

290

295

300

Glu Gly Lys Thr Leu Leu Asn Glu Lys Arg Ile Leu Asp Asp Lys Tyr
 305 310 315 320

Glu Gly Val Ala Phe Phe Lys Asn Pro Glu Gly Ile Ile
 325 330

<210> 28
 <211> 1161
 <212> DNA
 <213> Phlebotomus ariasi

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<210> 29
 <211> 137

<212> PRT

<213> Phlebotomus ariasi

<400> 29

Met His Phe Lys Ile Ile Phe Cys Ser Leu Phe Ile Val Leu Leu Gly
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His Met Ala Phe Ala Glu Ser Ser Glu Ser Ser Ser Ser Glu Ser Ser
 20 25 30

Ser Ser Glu Thr Ser Glu Glu Ser Ser Glu Glu Val Val Pro Ser Pro
 35 40 45

Ser Pro Ser Pro Lys His Arg Pro His Phe Gly Pro His His Pro His
 50 55 60

Gly Gly Arg Pro Lys Pro Pro His Pro Pro Pro Pro Lys Pro Glu Pro
 65 70 75 80

Glu Pro Asp Asn Gly Ser Asp Gly Gly Asn Gln Asp Asn Ser Asn Gly
 85 90 95

Gln Asp Asn Ser Asn Gly Asn Ser Gln Asn Asp Glu Gln Asp Asn Ser
 100 105 110

Gln Ser Gly Ser Ala Lys Arg Phe Arg Gln Pro Ala Val Asn Ile Val
 115 120 125

Asn Leu Val Ile Pro Phe Ser Thr Ile
 130 135

<210> 30

<211> 530

<212> DNA

<213> Phlebotomus ariasi

<400> 30

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 ctctcaatcg ggatccgcta agcgattcag acaacctgca gtgaatattg ttaatcttgt 420

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 ataataaaaa atacttttcag caaaaaaaaa aaaaaaaaaa aaaaaaaaaa 530

<210> 31
 <211> 170
 <212> PRT
 <213> Phlebotomus ariasi

<400> 31

Met Phe Ser Lys Ile Phe Ser Leu Ala Ile Leu Ala Leu Ala Leu Ser
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Thr Val Ser Ser Glu Thr Cys Ser Asn Pro Gln Val Lys Gly Ala Ser
 20 25 30

Ser Tyr Thr Thr Thr Asp Ala Thr Ile Val Ser Gln Ile Ala Phe Ile
 35 40 45

Thr Glu Phe Ser Leu Glu Cys Ser Asn Pro Gly Ala Glu Lys Val Ser

Leu Phe Ala Glu Val Asp Gly Arg Ile Thr Pro Val Ala Val Ile Gly
 65 70 75 80

Asp Thr Lys Tyr Gln Val Ser Trp Asn Glu Glu Val Lys Lys Ala Arg
 85 90 95

Ser Gly Asp Tyr Asn Val Arg Leu Tyr Asp Glu Glu Gly Tyr Gly Ala
 100 105 110

Val Arg Lys Ala Gln Arg Ser Gly Glu Glu Asn Asn Ala Lys Pro Leu
 115 120 125

Ala Thr Val Val Val Arg His Ser Gly Ser Tyr Thr Gly Pro Trp Phe
 130 135 140

Asn Ser Glu Ile Leu Ala Ser Gly Leu Ile Ala Val Val Ala Tyr Phe
 145 150 155 160

Ala Phe Ala Thr Arg Ser Lys Ile Leu Ser
 165 170

<210> 32
 <211> 674
 <212> DNA
 <213> Phlebotomus ariasi

<400> 32
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 ccaaattgcc ttcactactg aattctcact ggagtgtctg aatcccggag ctgagaaggt 240
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 aaaaaaaaaa aaaa 674

<210> 33
 <211> 250
 <212> PRT
 <213> Phlebotomus ariasi

<400> 33

Met Ser Asn Leu Leu Thr Ile Phe Gly Ala Ile Cys Phe Leu Gly Val
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Ala Asn Ser Leu Gln Phe Pro Arg Asn Pro Asp Gln Thr Arg Trp Ala
 20 25 30

Glu Lys Thr Cys Leu Lys Glu Ser Trp Ala Pro Pro Asn Leu Ile Asn
 35 40 45

Lys Trp Lys Gln Leu Glu Phe Pro Ser Thr Asn Leu Thr Tyr Cys Tyr
 50 55 60

Val Lys Cys Phe Val Met Tyr Leu Gly Val Tyr Asn Glu Thr Thr Lys
 65 70 75 80

Lys Phe Asn Val Asp Gly Ile Arg Ser Gln Phe Thr Ser Gln Gly Leu
 85 90 95

Arg Pro Pro Asn Gly Leu Glu Ser Leu Gln Lys Thr Ser Lys Gly Thr
 100 105 110

Cys Lys Asp Val Phe Arg Met Ser Ala Gly Leu Ile Lys Lys Tyr Lys
 115 120 125

Leu Glu Phe Val Lys Ala Phe His Gly Asp Ser Ala Glu Ala Ala Lys
 130 135 140

Trp Tyr Ile Glu His Lys Gly Asn Val Lys Ala Lys Tyr Gln Lys Ala
 145 150 155 160

Ser Glu Phe Cys Lys Thr Gln Lys Asp Glu Cys Arg Leu His Cys Arg
 165 170 175

Phe Tyr Tyr Tyr Arg Leu Val Asp Glu Asp Phe Gln Ile Phe Asn Arg
 180 185 190

Lys Phe Lys Ile Tyr Gly Ile Ser Asp Ser Gln Leu Arg Gln Cys Arg
 195 200 205

Ser Lys Ala Ser Gln Ala Lys Gly Cys Lys Val Ala Lys Val Leu Lys
 210 215 220

Asn Cys Leu Asp Lys Ile Asp Ser Glu Lys Val Lys Thr Ala Leu Lys
 225 230 235 240

Thr Leu Asp Glu Ile Ser Ala Asn Tyr Val
 245 250

<210> 34
 <211> 977
 <212> DNA
 <213> Phlebotomus ariasi

<400> 34
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 tacaagtcaa ggacttcgtc cacctaacgg tctagagagc ctacaaaaga catctaaagg 360
 aacctgcaag gatgtcttcc gaatgtccgc tggcctaate aagaagtaca aattggaatt 420
 cgtaaaagct ttccatggag attctgccga agctgcgaag tggtagatcg aacataaagg 480

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<210> 35
<211> 45
<212> PRT
<213> Phlebotomus ariasi

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<400> 35

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Met Tyr Phe Thr His Thr Leu Asn Phe Leu Leu Leu Val Ile Leu Leu
1           5           10           15

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Ile Met Ala Gly Phe Ser Gln Ala Asn Pro Glu Lys Arg Pro Cys Thr
          20           25           30

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Asn Cys Glu Arg Pro Lys Leu Ser Ala Lys Thr Pro Leu
          35           40           45

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<210> 36
<211> 346
<212> DNA
<213> Phlebotomus ariasi

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<400> 36
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ccctcaattt tcttcttctt gtaattctat taataatggc tggtttttcc caggcaaadc      120
ccgagaaaag gccctgcaca aactgtgagc gtcccaagtt atcggctaaa actcctttgt      180
aaccctttta aatcatataa tcggtgatta aagatttacc agcagagcta ccgcaatgtg      240
aaatcgaaaa attataccta cctacagaaa aactaaaaatg taataagaat tagaaaaaat      300
aaaaatgatc caagaacaaa aaaaaaaaaa aaaaaaaaaa aaaaaa      346

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<210> 37
<211> 232
<212> PRT

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<213> Phlebotomus ariasi

<400> 37

Met Thr Trp Val Ile Leu Cys Val Ala Leu Leu Val Ala Ser Val Val
1 5 10 15

Ala Glu Gly Gly Ile Asp Ala Glu Gly Asn Arg Thr Lys Ile Glu Lys
20 25 30

Ile Thr Ala Gly Ala Gly Ser Asp Gly Lys Val Val Tyr Thr Glu Gly
35 40 45

Gly Ser Phe Pro Glu Lys Leu Glu Lys Glu Gln Lys Ser Val Lys Lys
50 55 60

Glu Leu Gly Glu Leu Pro Lys Pro Thr Asn Ala Thr Phe Ser Pro Pro
65 70 75 80

Val Lys Val Glu Asn Lys Thr Glu Glu Val Arg Asn Ala Thr Leu Pro
85 90 95

Val Asn Ala Thr Thr Glu Ala Pro Lys Val Val Asn Thr Thr Ala Ser
100 105 110

Thr Thr Thr Val Lys Leu Thr Ser Thr Ser Thr Thr Thr Thr Pro
115 120 125

Lys Pro Lys Lys Pro Ser Leu Thr Ile Ser Val Glu Asp Asp Pro Ser
130 135 140

Leu Leu Glu Val Pro Val Lys Val Gln His Pro Gln Thr Gly Gly Arg
145 150 155 160

Leu Asp Val Glu Glu Pro Val Ala Gln Leu Ser His Glu Asn Ile Leu
165 170 175

Glu Met Pro Val Asn His Arg Asp Tyr Ile Val Pro Ile Val Val Leu
180 185 190

Ile Phe Ala Ile Pro Met Ile Leu Gly Leu Ala Thr Val Val Ile Arg
195 200 205

Arg Phe Arg Asp Tyr Arg Leu Thr Arg His Tyr Arg Arg Met Asp Tyr
210 215 220

Leu Val Asp Gly Met Tyr Asn Glu
225 230

<210> 38
<211> 899
<212> DNA
<213> Phlebotomus ariasi

<400> 38
atcgcgattc tggtgcaacg tcacagagta cttccttctt ttcctttcgg tttcctatca 60
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gcttccggtg tcgcggaggg cggaatcgat gcggagggga atcgcacgaa aatcgagaag 180
ataaccgcgg gtgcaggaag tgatggcaag gtggtctaca cagagggtgg aagcttcccc 240
gagaagctag agaaggagca gaagagcgtg aagaaggagc ttggagaatt gccaaagccc 300
acaaatgccca cattttcacc tcccgtgaag gtggagaata agacggagga ggtgaggaat 360
gctacactgc cggatgaatgc cacaactgag gcccttaagg tggtaatac gacagccagc 420
accaccacgg tgaagctaac atccaccagc accacaacaa ctactcccaa gcccaagaag 480
cccagcctca cgattagcgt ggaggacgat ccgagcctcc tggaggtgcc agtcaagggtg 540
cagcatccac agaccggagg acgactggat gtggaggagc ctgtgggtca gctgtcgcac 600
gagaacatcc tggagatgcc cgtgaatcac cgggactaca ttgttcccat tgtggtgctt 660
atctttgcca ttcccatgat cctgggactc gccactggtg tcatccgacg tttcagggac 720
taccggtca ctcgccacta ccgccggatg gactacctcg tggatggaat gtataatgag 780
tagtttccgg ctcgcactaa ccgcccaagc aataatctaa ttaatgctta atcgttttat 840
actatgtaaa taaatgtaca ttttaataat aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 899

<210> 39
<211> 65
<212> PRT
<213> Phlebotomus ariasi

<400> 39

Met Lys Lys Ile Leu Leu Phe Ser Val Ile Phe Val Ala Leu Leu Ile
1 5 10 15

Thr Ala Glu Ala Ile Pro Gly Lys Arg Ala Arg Pro Lys Ala Pro Ala
20 25 30

Val Thr Lys Gly Arg Asp Val Pro Lys Pro Arg Pro Gly Gln Gly Gly
35 40 45

Gln Val Pro Val Glu Pro Asp Phe Pro Met Glu Asn Leu Arg Ser Arg
 50 55 60

Ile
 65

<210> 40
 <211> 303
 <212> DNA
 <213> Phlebotomus ariasi

<400> 40
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 tgctttgttg atcactgccg aagccattcc gggaaaacgg gcaagaccga aagctcccgc 120
 ggtcactaaa ggtcgggatg ttccaaaacc aagacctggt caaggaggac aagtgccagt 180
 tgaaccagat tttcctatgg aaaacttaag aagtagaatt tagtagatct tcagctttct 240
 cggccccttt aataaaattc gtctactgat aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300
 aaa 303

<210> 41
 <211> 114
 <212> PRT
 <213> Phlebotomus ariasi

<400> 41

Met Ala Val Lys Asn Leu His Lys Phe Leu Leu Val Val Gly Phe Val
 1 5 10 15

Ser Leu Ile His Ala Ala Tyr Ser Ala Ala Gln His Arg Thr Tyr Leu
 20 25 30

Arg Ile Thr Glu Gln Glu Phe Asn Ser Leu Pro Phe Asp Ile Val Leu
 35 40 45

Gln Ala Val Val Ser Leu Ile Ile Leu Val Tyr Ser Ile Leu Gln Val

Val Gly Glu Phe Arg Glu Ile Arg Ala Ala Val Asp Leu Gln Ala Lys
 65 70 75 80

Ser Trp Glu Thr Leu Gly Asn Ile Pro Ser Phe Tyr Met Phe Asn His
 85 90 95

Arg Gly Lys Ser Leu Ser Gly Gln Tyr Glu Asp Asn Ile Asp Thr Ser
 100 105 110

Ala Asp

<210> 42
 <211> 536
 <212> DNA
 <213> Phlebotomus ariasi

<400> 42
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 ttcttgaaat ggcagttaaa aatcttcaca aattcctcct ggtcgtggga ttcgtgtccc 120
 tgatccatgc ggcttattcg gcagcacagc acagaacgta cctgagaatc acggagcagg 180
 agtttaattc tctcccattt gacattgtgc tccaagctgt ggtgagtctg atcattctgg 240
 tgtacagcat tctgcagggtt gttggggagt tccggggagat tcgagcagct gtggacttgc 300
 aagcgaaatc atggggagact ttgggtaaca tcccctcctt ctacatgttc aatcaccgtg 360
 ggaagagcct atccggccag tatgaggata acattgacac gagtgccgat tgaatgcccg 420
 gaagaagcct tcccgtaaat ctatttgaat gtaaggaatc cgattaattg aattaacacc 480
 aaaggagagc tgagggaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 536

<210> 43
 <211> 291
 <212> PRT
 <213> Phlebotomus ariasi

<400> 43

Met Met Ser Arg Trp Ser Lys Ser Val Lys Phe Val Cys Leu Leu Leu
 1 5 10 15

Cys Gly Gly Phe Thr Phe Leu Thr Thr Ser Ala Arg Ala Lys Pro Thr
 20 25 30

Leu Thr Phe Gln Leu Pro Pro Ala Leu Thr Asn Leu Pro Pro Phe Val
 35 40 45

Gly Ile Ser Arg Phe Val Glu Arg Lys Met Gln Asn Glu Gln Met Lys
 50 55 60

Thr Tyr Thr Gly Val Arg Gln Thr Asn Glu Ser Leu Val Met Ile Tyr
 65 70 75 80

His His Asp Leu Thr Ile Ala Ile Val Glu Leu Gly Pro Glu Lys Ser
 85 90 95

Leu Leu Gly Cys Glu Leu Ile Glu Ile Asn Asn Asp Asp Glu Gly Ala
 100 105 110

Lys Val Leu Lys Glu Leu Ala Thr Val Asn Ile Pro Leu Glu Ile Asp
 115 120 125

Phe Arg Glu Met Val Lys Leu Met Lys Gln Cys Glu Lys Ile Asp Tyr
 130 135 140

Ile Arg Lys Val Lys Arg Gln Gly Ala Pro Glu Ser Asp Gln Thr Thr
 145 150 155 160

Asn Arg Gln His Gln Thr Gly Tyr Phe Thr Gly Ala Thr Ala Gly Leu
 165 170 175

Ser Ile Leu Ser Gly Ile Leu Pro Gly Thr Lys Trp Cys Gly Thr Gly
 180 185 190

Asp Ile Ala Arg Thr Tyr His Asp Leu Gly Thr Glu Ala Thr Met Asp
 195 200 205

Met Cys Cys Arg Thr His Asp Leu Cys Pro Val Lys Val Arg Ser Tyr
 210 215 220

Gln Gln Arg Tyr Asn Leu Thr Asn Lys Ser Ile Tyr Thr Lys Ser His
 225 230 235 240

Cys Lys Cys Asp Asp Met Leu Phe Asn Cys Leu Lys Arg Thr Asn Thr
 245 250 255

Ser Ala Ser Gln Phe Met Gly Thr Ile Tyr Phe Asn Val Val Gln Val
 260 265 270

Pro Cys Val Leu Asp Thr Asp Arg Gly Tyr Arg Phe Arg Lys Ala Arg
 275 280 285

Thr Phe Ser
 290

<210> 44
 <211> 1087
 <212> DNA
 <213> Phlebotomus ariasi

<400> 44
 cacgaattag aaaacgggtcc cagtgattct ctcggtggct gatttataag agaatgtgaa

60

gagttgagga tgatgtctcg ctggagcaaa agtgtgaaat ttgtgtgcct cctcctgtgt 120
 ggcggattca cgtttctcac aacatcagca cgtgccaaac ccacactgac ctttcagcta 180
 ccgcccgcac tcacgaacct accccccttc gtgggcatct cacgattcgt cgaacgcaaa 240
 atgcagaatg agcagatgaa gacctacact ggcgttcggc agacgaatga gtctctcgtg 300
 atgatctacc accatgatct gacgatcgcc atcgtggaat tgggaccaga gaagagtctc 360
 ttgggttgtg aattgataga aattaacaac gatgacgaag gcgccaaagt gctgaaagaa 420
 ctggccacgg tgaatatacc actggagatc gacttccggg agatggtgaa gctcatgaag 480
 cagtgcgaga agatcgatta catacggaaa gtgaaacgcc aaggagcacc agagagtgc 540
 cagacgacaa atcgtcaaca ccagacgggc tacttcacgg gcgccactgc cggcctgagt 600
 atcctcagtg gcatccttcc cggcaccaag tgggtgtggca caggagacat cgccaggaca 660
 tatcacgatc tcggcacaga ggctaccatg gacatgtgct gtcgcactca cgatctctgt 720
 ccagtgaaag tgcgctcata tcagcaacgc tacaatctca ccaataagtc aatctacaca 780
 aaatctcact gtaaagtga tgacatgctg ttcaattgcc tcaagaggac caacacgtca 840
 gcctcgcaat tcatggggac catctacttc aacgtgggtcc aagtgccatg tgttctggac 900
 acagacagag gctacagatt cagaaaagcg agaaccttct cctgatcatc gcaatgcaac 960
 attttcagct gaggtgctct ttcaaagaa ttatttatat gttacaaaaa aaaaaaaaaa 1080
 aaaaaaa 1087

<210> 45

<211> 139

<212> PRT

<213> Phlebotomus ariasi

<400> 45

Met Lys Leu Leu Pro Ile Ile Leu Leu Ala Leu Thr Val Leu Ile Val
 1 5 10 15

Thr Cys Gln Ala Glu His Pro Gly Thr Lys Cys Arg Arg Glu Phe Ala
 20 25 30

Ile Glu Glu Glu Cys Ile Asn His Cys Glu Tyr Lys His Phe Gly Phe
 35 40 45

Thr Asp Asp Gln Phe Arg Ile Lys Lys His His Arg Glu Asn Phe Lys
 50 55 60

Asn Ala Met Ser His Tyr Gly Ala Ile Arg Lys Asp Gln Glu Gly Glu
 41

65 70 75 80

Leu Asp Lys Leu Leu Asn Arg Cys Ala Lys Lys Ala Lys Glu Ser Pro
 85 90 95

Ala Thr Ser Lys Arg Asp Lys Cys Tyr Arg Ile Ile Asn Tyr Tyr Arg
100 105 110

Cys Val Val Val Asp Asn Asn Leu Ile Asn Tyr Ser Val Tyr Val Lys
115 120 125

Ala Val Thr Lys Ile Asn Asp Ser Ile Asn Val
130 135

<210> 46
<211> 518
<212> DNA
<213> *Phlebotomus ariasi*

[illegible]

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<210> 47
<211> 137
<212> PRT
<213> Phlebotomus ariasi
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<400> 47

Met Lys Glu Leu Val Val Phe Leu Thr Leu Ile Val Leu Val Val Ile
1 5 10 15

Cys His Ala Glu Arg Pro Ser Gln Lys Cys Arg Arg Glu Leu Lys Thr
20 25 30

Glu Glu Glu Cys Ile Leu His Cys Glu Tyr Lys His Tyr Arg Phe Thr
42

35

40

45

Asp Asp Gln Phe Arg Leu Asn Ala Asp Gln Arg Gly Asp Phe Arg Asn
 50 55 60

Ile Met Arg Arg Tyr Gly Ala Ile Arg Val Asp Gln Glu Ser Gln Leu
 65 70 75 80

Asp Lys His Leu Lys Lys Cys Ala Asn Lys Val Ala Lys Thr Pro Ala
 85 90 95

Thr Ser Arg Lys Asp Lys Cys Arg Lys Ile Ser Arg Tyr Tyr His Cys
 100 105 110

Ala Val Asp Asn Lys Leu Phe Lys Tyr Asn Asp Tyr Ala Asn Ala Ile
 115 120 125

Ile Lys Tyr Asp Lys Thr Ile Asn Val
 130 135

<210> 48
 <211> 507
 <212> DNA
 <213> Phlebotomus ariasi

<400> 48
 atagaaatcg aatcatgaag gagcttggtg tatttttgac actgatagtt ttggctcgtga 60
 tttgtcacgc agaacgacct tcacaaaagt gtaggaggga actgaagaca gaggaagagt 120
 gtatactgca ttgtgagtac aaacattatc gctttactga tgaccagttt cgacttaacg 180
 cagatcaaag aggagacttt aggaatatca tgaggaggta cggcgcaatt aggggtggatc 240
 aggaaagtca attggataag catttgaaaa aatgtgccaa caaagttgct aagactccgg 300
 caacatcgag gaaggataag tgtaggaaaa tttctcggta ctatcactgt gctgtggata 360
 ataaactttt caaatataat gattatgcc aatgccataat taaatatgat aagacaataa 420
 atgttttaaag atgaatgtat cgctcaaata aagaagcaaa gctaaccata ttcaaataa 480
 aaaaaaaaaa aaaaaaaaaa aaaaaaa 507

<210> 49
 <211> 393
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 49

Met Lys Ile Phe Leu Cys Leu Ile Ala Val Val Phe Leu Gln Gly Val

[illegible]

245

250

255

Ser Thr Lys Leu Phe Glu Ile Ser Thr Lys Ile Leu Lys Glu Lys Gly
 260 265 270

Ala Lys Phe Asp Pro Val Asn Leu Gly Asn Arg Gly Pro His Thr Glu
 275 280 285

Ala Val Ala Leu Val Tyr Asp Pro Lys Thr Lys Val Ile Phe Phe Ala
 290 295 300

Glu Ser Asp Ser Arg Gln Val Ser Cys Trp Asn Thr Gln Lys Pro Leu
 305 310 315 320

Asn His Lys Asn Thr Asp Val Ile Phe Ala Ser Ala Lys Phe Ile Tyr
 325 330 335

Gly Ser Asp Ile Ser Val Asp Ser Glu Ser Gln Leu Trp Phe Leu Ser
 340 345 350

Thr Gly His Pro Pro Ile Pro Asn Leu Lys Leu Thr Phe Asp Lys Pro
 355 360 365

His Ile Arg Leu Met Arg Val Asp Thr Ala Lys Ala Ile Arg Arg Thr
 370 375 380

Arg Cys Glu Val Lys Pro Arg Lys Pro
 385 390

<210> 50

<211> 1341

<212> DNA

<213> Phlebotomus perniciosus

<400> 50

tatatataac ttttgaaatg ttcagtcagt cttttggaag caaagatgaa gatctttctg 60
 tgcctaattg ctgtgggtttt ctttcaggga gttgtaggct ttcacgttga acgagaatat 120
 gcgtggaaaa acattagtta cgaaggagta gatccagcat tattcaatat tgataatattc 180
 attccgactg gtttcgttca cgatgcaatt aataagaaga ttttcattgc tgttccaagg 240
 agatctcctc aaataccatt taccctaact gaacttgata ccaccaagca tccggaacgt 300
 tctcctcctc taagcaaatt tcttggtagc gataaattaa tcaacgttta tcaaccggtc 360
 attgacgaat gtcgccgact ttggattgac gacgtcggac gggttgacta caagggggat 420
 gagcagaagt atccaaacca aaatgctgtt ctcatagctt atgacctgac gaaggaaaat 480

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taccagaga ttcacgata cgagatacca agtaaaattg ctgggtcaaa tacaattcca      540
tttgaggat ttgccgttga tgttacgaat ccgaaggagg gatgcggcaa aacctttgtc      600
tacatcacga acttcgaaga caacactctg atttgtgtacg atcaggagaa gaaagattct      660
tggaagatca gtcatgggtc attcaaacca gagcatgact cgactctctc ccatgacggt      720
aaacagtaca agtatagagt ggggtttattc ggaattactc ttggagatcg ggatccggaa      780
ggaaatcgtc cggcttacta catagccgga agcagtacga agctctttga gatcagcact      840
aagattttga aggagaaggg tgccaaattt gatcctgtta atttgggaaa tcgtgggtccc      900
cacactgaag ctggtgccct ggtatatgat cccaagacaa aagttatctt ctttgttgaa      960
tctgactcca ggcagggtctc ttgctggaat acccagaagc cactgaatca taagaacact     1020
gatgtgattt ttgccagtgc caaatttatt tacgggtccg atatttcagt tgatagttaa     1080
tctcaattgt ggttcttatt cacgggacat ccacccattc ctaatctcaa gttgaccttt     1140
gataaacccc atattcgtct tatgagggtg gatacggcta aagcaattcg tagaactaga     1200
tgcaagtga agccccgcaa gccataagac gaatatctaa tatcaaaaat gttacaattc     1260
tgctaaaatg tctaaaaata aagataataa taaataaata aaaatattgt gcaacacaca     1320
gaaacaaacc aaaaaaaaaa a                                             1341

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<210> 51
 <211> 388
 <212> PRT
 <213> *Phlebotomus perniciosus*

<400> 51

Met Lys Ile Phe Leu Cys Leu Ile Ala Val Val Ser Leu Gln Gly Val
 1 5 10 15

Leu Ala Tyr Asp Ile Glu Arg Glu Tyr Ala Trp Lys Asn Ile Ser Phe
 20 25 30

Glu Gly Ile Asp Pro Ala Ser Tyr Ser Val Lys Asn Ser Ile Val Thr
 35 40 45

Gly Phe Ala His Asp Ala Asp Ser Lys Lys Ile Phe Ile Thr Ile Pro
 50 55 60

Arg Leu Asn Pro Val Pro Ile Thr Leu Thr Glu Leu Asp Thr Thr Lys
 65 70 75 80

His Pro Glu Gly Ser Pro Pro Leu Ser Lys Phe Pro Gly Ser Asp Lys
 85 90 95

Leu Ile Ser Val Tyr Gln Pro Val Ile Asp Glu Cys Arg Arg Leu Trp
 100 105 110

Ile Val Asp Ala Gly Gln Val Glu Tyr Lys Gly Asp Glu Gln Lys Ile
 115 120 125

Pro Lys Lys Asn Ala Ala Ile Ile Ala Tyr Asp Leu Thr Lys Asp Asn
 130 135 140

Tyr Pro Glu Ile Asp Arg Tyr Glu Ile Pro Asn Asn Val Ala Gly Asn
 145 150 155 160

Pro Leu Gly Phe Gly Gly Phe Ala Val Asp Val Thr Asn Pro Lys Glu
 165 170 175

Gly Cys Gly Lys Thr Phe Val Tyr Ile Thr Asn Phe Glu Asp Asn Thr
 180 185 190

Leu Ile Val Tyr Asp Gln Glu Lys Lys Asp Ser Trp Lys Ile Ser His
 195 200 205

Asp Ser Phe Lys Pro Glu His Glu Ser Ile Leu Thr His Asn Gly Ala
 210 215 220

Gln His Ile Leu Lys Leu Gly Ile Phe Gly Ile Thr Leu Gly Asp Leu
 225 230 235 240

Asp Glu Glu Gly Asn Arg Gln Ala Tyr Tyr Leu Gly Gly Ser Ser Thr
 245 250 255

Lys Leu Phe Arg Val Asn Thr Lys Asp Leu Lys Lys Lys Ala Gly Gln
 260 265 270

Ile Glu Phe Thr Pro Leu Gly Asp Arg Gly Ser His Ser Glu Ala Leu
 275 280 285

Ala Leu Ala Tyr Asp Pro Lys Thr Lys Val Ile Phe Phe Ile Glu Tyr
 290 295 300

Asn Ser Lys Arg Ile Ser Cys Trp Asn Thr Gln Lys Ser Leu Asn Pro
 305 310 315 320

Asp Asn Ile Asp Val Ile Tyr His Ser Pro Asp Phe Ile Phe Gly Thr
 325 330 335

Asp Ile Ser Met Asp Ser Glu Ser Lys Leu Trp Phe Phe Ser Asn Gly
 340 345 350

His Pro Pro Ile Glu Asn Val Gln Leu Thr Phe Asp Lys Pro His Phe
 355 360 365

Arg Leu Ile Ser Met Asp Thr Lys Lys Ser Ile His Gly Thr Lys Cys
 370 375 380

Glu Val Lys Pro
 385

<210> 52
 <211> 1273
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 52
 caagatgaaa atctttctgt gcctaattgc tgtggtttcc cttcagggag ttttagctta 60
 tgatattgag aggggaatacg cgtggaaaaa catcagtttt gaaggaatag acccagcatc 120
 ctacagcggt aaaaatagta tcgtaactgg tttcgctcac gatgcagata gtaagaagat 180
 tttcattact attccaaggc taaaccagc tccgattact ctaactgaac tggataccac 240
 taagcatccg gaaggatctc ctccactaag caaatttcct ggtagtgata aattaatctc 300
 tgtttatcaa ccggtcattg acgaatgtcg ccgactttgg attgtggacg ctggacaggt 360
 tgagtacaaa ggagatgagc agaagattcc caagaaaaat gctgctatta tagcttatga 420
 tctgacgaag gacaattatc cagaaattga tcgatacgag ataccgaata atgttgctgg 480
 taatccactt ggatttgagg gatttgccgt tgatgttaca aatccgaaag agggatgtgg 540
 taaaaccttt gtctacatca cgaacttcga agacaacact ctaatagtgt atgatcagga 600
 gaagaaagat tcctggaaga tcagtcatga ttcattcaaa cctgagcatg aatcgatcct 660
 gaccacaac ggtgctcaac acatttttaa gttgggtata ttcggaatca ccttaggaga 720
 tctggatgag gagggaaatc gtcaggctta ctacttgga ggtagtagta cgaagctctt 780
 tagagtgaac accaaggatc tcaagaagaa agccggtcaa attgaattca ctctctggg 840
 agatcgtgga tctcactctg aagcccttgc tctggcttat gatcccaaga ctaaagttat 900
 ctttttcatt gaatataatt ctaagcgaat ctctgctgg aacactcaga aatcactaaa 960
 tcctgacaac attgatgtga tttatcacag tcctgatttt atcttcggca ctgatatttc 1020
 aatggatagt gaatccaaat tgtggttctt ttccaacggt catccaccaa ttgagaatgt 1080

tcaactaact ttgataagc cacattttcg tcttataagc atggatacga aaaaatcaat 1140
 tcatgggtact aaatgcgaag taaaacctta agtcaaactt ggaaaataaa acactttctta 1200
 aagaaattgt aatttttatg atggtaataa atttttgtgt gccgaaaaaa aaaaaaaaaa 1260
 aaaaaaaaaa aaa 1273

<210> 53
 <211> 208
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 53

Met Phe Lys Lys Phe Ile Leu Val Ala Leu Val Val Val Val Ala Gln
 1 5 10 15

Cys Ala Leu Pro Ala Ile Pro Ile Ala Arg Gln Gly Lys Asp Phe Pro
 20 25 30

Val Pro Phe Val Ser Glu Asp Asn Asn Pro Asp Asp Tyr Phe Asp Asp
 35 40 45

Gln Tyr Tyr Pro Asp Ile Asn Asp Ala Gly Val Gly Ser Lys Ala Pro
 50 55 60

Gln Gly Ser Arg Lys Pro Pro Asn Arg Gly Thr Ile Pro Pro Pro Arg
 65 70 75 80

Gly Asp Gln Val Ser Ser Gly Gly Arg Thr Pro Pro Gly Arg Val Gly
 85 90 95

Gln Gly Thr Ser Pro Thr Lys Asp Lys Arg Ala Arg Pro Gln Ile Asn
 100 105 110

Arg Asn Pro Thr Gly Thr Val Gly Gln Gly Gly Ser Pro Gly Thr Lys
 115 120 125

Asp Lys Arg Ala Arg Pro Gln Ile Asn Arg Asn Pro Thr Gly Ser Gly
 130 135 140

Thr Lys Pro Arg Asp Arg Glu Leu Val Ile Arg Asp Lys Pro Pro Ser
 145 150 155 160

Gly Ser Gln Gly Gly Lys Pro Gly Arg Gln Val Arg Gly Pro Lys Glu
 165 170 175

Asp Leu Ser Arg Tyr Gln Asn Ala Pro Ala Lys Leu Ile Phe Lys Ser

180

185

190

Ser Asn Ile Asn Thr Ala Gly Lys Thr Pro Lys Arg Cys Glu Val Val
 195 200 205

<210> 54
 <211> 954
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 54
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 gtcgtggcac aatgtgctct tcccgcaatc ccaattgcaa gacagggaaa agatttcccc 120
 gtcccgtttg taagtgaaga taataatccg gatgattatt ttgacgatca gtactatccg 180
 gacataaacg atgcgggtgt aggttcaaag gctccgcagg gaagcagaaa gccacccaat 240
 agaggcacca tccctcctcc tcgtggtgac caagtgtcat ctggtggacg aactccaccc 300
 ggaagggttg gacagggtac aagccctaca aaggataaaa gagctcgtcc tcagattaac 360
 agaaacccaa ccggaacggt tggacagggt ggaagccctg gtacaaagga taaaagagct 420
 cgtcctcaga ttaacagaaa cccaaccgga agtgggtacaa aaccagaga tagggagctt 480
 gtgattaggg ataagcccc atccggaagt caaggtggtta aacctggaag acaggtcaga 540
 ggcccaaagg aagatttgtc gcgttatcaa aacgctccgg caaagttgat tttcaaactc 600
 agtaatatca atactgctgg taaaaccccg aagcgtgtg aagttgttta agacgaagaa 660
 ggacaaaaca gttgttgcta agggagggtcc caacgatgtt tatgaggtgg agcttctcga 720
 tggaaatttc aataatatga gcttgaggat ccagataatg gacaggaaga gcagcacagc 780
 gatcctcagc aatccagatc gcaacttaat tggtggccgt gtcaagacgt accgcggatt 840
 aagatgaggt gctgaatttt taaattttat tttatttttt tgctcctaaa tccaaaatcc 900
 ccccaaataa atcagtttga acgcaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 954

<210> 55
 <211> 310
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 55

Met Thr Tyr Phe Lys Ile Ser Thr Cys Cys Leu Val Leu Ile Ser Leu
 1 5 10 15

Ile Leu Pro Ile Ile Cys Ile Lys Val Ile Arg Phe Asp Asp Arg Asp
 20 25 30

Glu Tyr Leu Leu Gly Lys Pro Asp Asn Thr Asp Glu Glu Leu Leu Tyr
 35 40 45
 Ser Thr Phe Asp Phe Ile Lys Asn Thr Cys Ala Asn Pro Lys Met Lys
 50 55 60
 Cys Thr Asn Asn Ala Thr His Phe Val Leu Asp Phe Ser Asp Pro Lys
 65 70 75 80
 Lys Arg Cys Ile Ser Ser Ile His Val Phe Ser Thr Pro Asp Gly Pro
 85 90 95
 Val Asn Leu Glu Glu Glu Asn Lys Pro Arg Ser Lys Ser Ser Ile Tyr
 100 105 110
 Cys Gln Val Gly Gly Ile Gly Gln Ser Tyr Cys Leu Leu Val Phe Lys
 115 120 125
 Lys Lys Glu Arg Arg Glu Asp Ala Leu Val Asp Ile Arg Gly Leu Lys
 130 135 140
 Thr Cys Ser Leu Lys Glu Arg Tyr Thr Ser Gly Asp Pro Lys Lys Thr
 145 150 155 160
 Asp Ala Tyr Gly Met Ala Tyr Lys Phe Asp Lys Asn Asp Asn Trp Ser
 165 170 175
 Ile Lys Arg Glu Gly Val Lys Gln Trp Lys Arg Ser Gly Asn Glu Ile
 180 185 190
 Phe Tyr Arg Lys Asn Gly Leu Met Asn His Gln Ile Arg Tyr Leu Ser
 195 200 205
 Lys Phe Asp Lys Tyr Thr Val Thr Arg Glu Met Val Val Lys His Arg
 Ala Lys Lys Phe Thr Met Asp Phe Ser Asn Tyr Gly Gln Tyr Arg Ile
 225 230 235 240
 Ser Phe Leu Asp Val Tyr Trp Phe Gln Glu Ser Val Lys His Lys Pro
 245 250 255
 Lys Leu Pro Tyr Ile Tyr Tyr Asn Gly Glu Cys Leu Pro Ser Asn Lys
 260 265 270

Thr Cys Gln Leu Val Phe Asp Ala Asp Glu Pro Ile Thr Tyr Ala Phe
 275 280 285

Val Lys Val Phe Ser Asn Pro Asp His Asn Glu Pro Arg Leu Arg His
 290 295 300

Ala Asp Leu Gly Arg Gly
 305 310

<210> 56
 <211> 1081
 <212> DNA
 <213> *Phlebotomus perniciosus*

<400> 56
 ggccattacg gccaggggga ataagttagt gtcttcacgt ttattgaagc tttcacttca 60
 atatgactta cttcaagatc agtacttggt gtttagtttt aataagcctc attctaccta 120
 taatttgat taaagttatt cgttttgatg atagagatga atatcttctt ggtaaacctg 180
 ataatactga tgaagaactc ctctattcaa cctttgactt cattaagaat acctgcgcta 240
 atcctaaaat gaaatgcacc aataacgcca ctcatctcgt tctggatttc tctgatccga 300
 agaagagatg tatctctccc atccatgtat tttccactcc cgatggacct gttaatcttg 360
 aggaggagaa taagcctcga tcaaagagtt caatttactg ccaagtgggc ggcattggac 420
 agagttactg tttgctggtg tttaaaaaga aggaacgtcg tgaggatgct ctgggtgata 480
 tccggggact caaaacatgc tccctcaagg agcgtacac atctggagat cccaagaaaa 540
 ccgatgctta cggaatggca tacaattcg acaagaatga taattggagc atcaagagag 600
 aaggtgttaa gcaatggaaa agatcaggaa atgagatctt ctaccgcaag aatggtttga 660
 tgaaccatca aataagatac ttgagcaagt ttgataagta cacggttacc agagaaatgg 720
 tcgtgaagca ccgcgctaag aaattcacca tggacttctc caactatggc cagtacagaa 780
 tcagtttctt ggacgtctac tggttccagg agtccgtgaa gcacaagccg aagttaccct 840
 acatctacta caatggcgaa tgcttgccca gcaataagac gtgtcagttg gttttcgacg 900
 ctgatgagcc tattacttat gcttttgtga aagtgttcag taatccggac cacaacgaac 960
 cacgattgag gcatgcagat ctgggacgag gataggagtg gattagtccg ttgttgaaat 1020
 ttgaataaaa tgctatgaag atgttaaatt tgcctcaaaa aaaaaaaaaa aaaaaaaaaa 1080
 a 1081

<210> 57
 <211> 431
 <212> PRT

<213> Phlebotomus perniciosus

<400> 57

Met Lys Leu Leu Ile Thr Ile Gly Ala Val Cys Val Leu Gln Val Val
 1 5 10 15
 Thr Val Ser Ser Ile Phe Phe Pro Ile Pro Ile Asn Ile Gln Thr Gly
 20 25 30
 Thr Thr Ser Ser Ser Ser Gly Gln Pro Gly Gln Gln Val Thr Thr Ser
 35 40 45
 Ile Ser Phe Ser Asn Val Ser Asn Ile Thr Asp Met Val Ile Tyr Leu
 50 55 60
 Thr Gln Asn Ile Ser Arg Ala Leu Leu Thr Arg Val Pro Asn Pro Asp
 65 70 75 80
 Asp Ile Lys Ser Ala Ala Asp Ile Leu Glu Ser Phe Thr Gly Ser Leu
 85 90 95
 Lys Tyr Phe Gln Thr Pro Pro Asp Asp Val Asp Gln Glu Glu Ser Glu
 100 105 110
 Thr Lys Ser Arg Ser Lys Arg Ser Phe Thr Asp Ile Phe Lys Gln Ser
 115 120 125
 Ser Pro Leu Lys Glu Ile Gly Glu Arg Ile Glu Glu Ile Lys Lys Lys
 130 135 140
 Leu Lys Gly Met Leu Lys Pro Lys Pro Gln Thr Pro Ser Gly Asn Gln
 145 150 155 160
 Thr Asp Ser Ser Asn Thr Thr Ser Glu Thr Gln Ser Arg Lys Lys Arg
 165 170 175
 Ala Leu Thr Asp Phe Ile Pro Met Asp Ser Leu Lys Asp Ala Ile Ser
 180 185 190
 Lys Thr Gly Glu Val Leu Ile Pro Ser Ser Ala Ser Ala Asn Ser Ser
 195 200 205
 Pro Leu Asp Phe Met Ser Lys Leu Ser Asp Ile Ala Asn Asp Leu Ile
 210 215 220

Gln Asn Ser Met Lys Glu Ile Ser Glu Asn Leu Ala Ser Ser Val Ala
 225 230 235 240

Met Tyr Gln Val Asn Ser Gln Leu Asp Ala Ile Lys Gln Ser Met Asp
 245 250 255

Ile Ile Lys Gln Glu Ile Asp Lys Thr Gln Lys Ile Gln Lys Tyr Val
 260 265 270

Lys Glu Ala Leu Asn Gln Ala Lys Asn Ala Thr Lys Ser Leu Gly Glu
 275 280 285

Lys Leu Lys Ser Ser Asn Cys Phe Ala Gln Phe Ile Asn Pro Phe Lys
 290 295 300

Leu Phe Glu Lys Gly Ile Thr Cys Val Lys Asn Lys Ile Asp Asn Gly
 305 310 315 320

Leu Lys Ile Ala Lys Asp Thr Phe Lys Asn Leu Gln Gln Ala Met Ser
 325 330 335

Val Pro Ser Asp Ile Gln Ser Glu Val Ser Lys Cys Ser Gln Asn Gln
 340 345 350

Gln Leu Asn Pro Ile Ala Lys Leu Leu Cys Tyr Leu Arg Thr Pro Leu
 355 360 365

Gln Leu Asp Asp Glu Lys Leu Leu Leu Pro Phe Glu Phe Thr Arg Arg
 370 375 380

Ile Arg Glu Ile Thr Asn Tyr Phe Ala Thr Met Arg Met Asp Leu Ile
 385 390 395 400

Arg Cys Gly Ile Glu Thr Ile Gln Ser Ile Gly Asp Lys Val Glu Asp
 405 410 415

Cys Ala Arg Glu Ala Ile Leu Ala Val Lys Asp Thr Leu Lys Gly
 420 425 430

<210> 58

<211> 1471

<212> DNA

<213> Phlebotomus perniciosus

<400> 58

aaaacatctt cgcgttttcg tgctatttga aacggagaac atcgagtaaa gaatatgaag

60

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ttactaatta ctatcgggtgc ggtttgtgtg ttacaagtcg ttacagtatc atccatcttc      120
tttcccattc caatcaacat ccaaacaggg acgacatcat catcatcagg acaaccagga      180
cagcaagtta caacgagtat aagtttcagt aatgtatcaa acatcacgga tatggtgatt      240
tatctcacgc agaatatcag tagagctctc cttacgcgtg taccaaacc tgaatgatatc      300
aatcagcag cggatatctt ggaaagtttt acaggaagcc tcaagtattt ccaaacacct      360
ccggatgatg tggatcaaga ggaatcagag acaaagtcac gatctaagag atcatttact      420
gatatattca aacaatcttc gccttttaaaa gaaatcggag aaaggatcga agaaataaaa      480
aagaaactaa aaggaatgct caaaccaaaa ccgcaaacac cttctggaaa tcaaactgat      540
agctcgaaca caacttcgga gactcaatcg agaaagaaac gggctttaac tgactttata      600
ccaatggatt ctctgaaaga tgcgatttca aaaacagggg aagtgttgat accttcaagt      660
gcaagtgcaa actctagtcc tctagatttt atgtcaaaac tatccgatat cgcaaatgat      720
cttattcaaa actcaatgaa ggaaatctcc gaaaatttag cctcaagcgt tgctatgtac      780
caagtcaact cacagttaga tgccattaaa caatccatgg atattataaa acaagaaatt      840
gataagaccc aaaagatcca gaaatacgtg aaggaagctc ttaatcaagc caaaaatgct      900
actaaatctt taggagaaaa gcttaagtcc agtaactgtt tcgctcaatt tataaatccc      960
tttaaacttt ttgaaaaagg aattacttgt gtgaaaaata aaatcgataa tggattaaaa     1020
atcgcaaaag acacctttta gaatttaca caggcaatga gtgtgccctc agatattcaa     1080
agtgaagtgt ccaaagctc ccaaatacag caattgaatc ccattgccaa actcctgtgc     1140
tacttgagga caccactgca attggacgac gagaagttgc tgcttccctt tgaatttacg     1200
aggagaatta gagaaataac taactatttt gccaccatga gaatggacct cattcgttgt     1260
ggcatagaaa ctattcagtc gatcggagac aaggttgagg attgtgcaag agaagcaata     1320
ttggctgtaa aggacactct gaagggataa agtccgcatt ttctggctgt ccaattggga     1380
ctaaccat cattgatgat gccgagctat tgtatgttgg agaaaatgaa taaaaggctt     1440
cgcaaaaaaa aaaaaaaaaa aaaaaaaaaa a

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<210> 59
 <211> 131
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 59

Met Lys Gln Leu Val Val Phe Leu Ala Leu Ile Val Leu Ile Val Ile

1

5

10

15

Cys His Ala Glu Pro Pro Ser Lys Lys Cys Arg Ser Gly Leu Val Lys
 20 25 30

Asp Glu Glu Cys Ile Leu His Cys Glu Tyr Lys Tyr Tyr Gly Phe Thr
 35 40 45

Asp Asp Asn Phe Glu Leu Asp Ser Asp Leu Arg Gly His Phe Arg Thr
 50 55 60

Ala Met Arg Lys His Gly Ala Ile Arg Ile Asp Gln Glu Arg Gln Leu
 65 70 75 80

Asp Lys His Leu Lys Lys Cys Ala Gln Glu Ala Lys Lys Ser Glu Lys
 85 90 95

100

105

110

Phe Gln Tyr Asn Ala Tyr Ala Lys Ala Ile Ile Ala Leu Asp Lys Thr
 115 120 125

Ile Asn Val
 130

<210> 60
 <211> 499
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 60
 attagaaaac caatcatgaa gcagcttggt gtatttttgg cgttgatagt tctgatagtg 60
 atttgtcacg cagaaccacc ttcgaagaag tgtaggagtg gactggtgaa agatgaggag 120
 tgtatactcc attgtgaata caaatactat ggctttactg atgataattt cgaacttgat 180
 tcagatctaa gaggacactt tagaactgct atgaggaagc acggcgcaat taggatcgat 240
 caggaaagac aacttgataa gcatttgaaa aaatgtgctc aggaagctaa aaagtcggaa 300
 aagtgtagga aaatcattca gtactatcgc tgtgctgtga ataataaact tttccaatat 360
 aatgcttatg ctaaagcaat tattgcgctt gataagacaa taaatgttta aaaaagaaag 420
 tgaaatgtat ctatcgctca aataaagaag gaagctaaga tcgttgaaag aaaaaaaaaa 480
 aaaaaaaaaa aaaaaaaaaa 499

<210> 61
 <211> 388
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 61

Met Ile Asn Ser Thr Val Ile Gln Phe Ile Phe Leu Phe Val Ile Phe
1 5 10 15

Leu Pro Gly Lys Ser Lys Ser Ala Pro Lys Thr Cys Glu Ile Asn Leu
20 25 30

Pro Thr Ser Ile Pro Thr Lys Gly Glu Ser Ile Tyr Leu Leu Asn Gly
35 40 45

Asn Gly Ser Val Phe Arg Pro Asp Gly Lys Leu Thr Gln Leu Asn Ile
50 55 60

Gly Asp Ser Leu Ser Ile Tyr Cys Pro Gly Gln Lys Glu Leu Lys Arg
65 70 75 80

Val Pro Cys Ser Pro Lys Phe Ser Leu Glu Asn Ile Thr Cys Asn Ser
85 90 95

Asn Val His Ser Glu Leu Val Asp Thr Glu Glu Lys Cys Gly Lys Asp
100 105 110

Gly Lys Cys Tyr Asn Ile Ser Phe Pro Leu Pro Thr Asn Thr Phe His
115 120 125

Thr Ile Tyr Arg Thr Cys Phe Asn Lys Gln Lys Leu Thr Pro Ile Tyr
130 135 140

Ser Tyr His Val Ile Asn Gly Lys Ala Val Gly Tyr His Val Lys Gln
145 150 155 160

Pro Arg Gly Asn Phe Arg Pro Gly Lys Gly Val Tyr Arg Lys Ile Asn
165 170 175

Ile Asn Glu Leu Tyr Lys Thr His Ile Ser Arg Phe Lys Arg Ile Ile
180 185 190

Gly Ser Thr Gln Thr Phe Phe Arg Lys Pro Leu His Tyr Leu Ala Arg
195 200 205

Gly His Leu Ser Pro Glu Val Asp Phe Val Phe Gly Asn Glu Gln His
210 215 220

Ala Thr Glu Phe Tyr Ile Asn Thr Ala Pro Gln Tyr Gln Ser Ile Asn
57

225 230 235 240

Gln Gly Asn Trp Leu Arg Val Glu Lys His Val Arg Lys Leu Ala Lys
245 250 255

[illegible]

Lys Phe Ser Asn Lys Arg Ala Glu Arg Glu Ile Tyr Leu Gly Glu Gly
275 280 285

Val Ile Pro Val Pro Gln Ile Phe Trp Lys Ala Val Phe His Pro Lys
290 295 300

Thr Ser Ser Ala Ile Val Phe Val Ser Ser Asn Asn Pro His Glu Lys
305 310 315 320

Thr Phe Asn Pro Met Cys Lys Asp Val Cys Glu Thr Ala Arg Phe Gly
325 330 335

Gly Lys Gln His Glu Asn Gln Asn Phe Ser Asn His Thr Val Gly Phe
340 345 350

Thr Ile Cys Cys Glu Leu Pro Asp Phe Leu Gly Asn Ser Lys Val Ile
355 360 365

Leu Pro Lys Glu Phe Gln Gly Lys Asn Tyr Arg Lys Leu Leu Lys Met
370 375 380

Pro Gly Lys Pro
385

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<210> 62
<211> 1772
<212> DNA
<213> Phlebotomus perniciosus
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<400>	62						
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tctttttgtg	atttttcttc	ctggaaaatc	taaaagtgcc	ccaaagactt	gcgaaattaa	120	
tcttcccacc	agtattccga	caaaagggtga	atcaatttat	cttctcaatg	gaaatggatc	180	
ggtcttccga	ccggatggaa	aattgactca	actcaatatt	ggggattccc	tgtccatcta	240	
ctgtcctgga	cagaagggagc	tcaagagagt	cccttgcagt	cccaaatttt	cccttgagaa	300	
catcacttgc	aacagcaatg	ttcacagtga	attggttgac	acggagggaaa	agtgcggaaa	360	

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agatggaaaa tggtacaata ttagctttcc attgccaaca aataccttcc atacaatcta      420
cagaacttgc ttcaacaagc agaaactaac accaatctat tcttatcacg tcatcaatgg      480
aaaggcagtt ggatatcatg tgaaacagcc acgaggaaac tttcgaccgg gaaaagggtgt      540
ctacaggaag atcaacatca atgagctcta caagaccac atttcgcgct tcaagagaat      600
catcggatcc acccagacat tcttccggaa gccctgcac tatctggctc gtggacatct      660
ctcacctgaa gtggactttg tctttggcaa cgaacaacac gccactgagt tctacatcaa      720
caccgcccc caatatcaat ccatcaacca gggaaattgg cttcgagtgg agaaacacgt      780
gcgcaaactg gccaaaggccc tccaggatga tctccacgtt gtcactggaa ttttgggcat      840
cctcaagttc tcaaacaac gagccgaaag agaaatctat ctgggcgaag gagttattcc      900
tgtaccgcaa atattttgga aggtgtctt ccaccctaaa acctcttccg ccattgtctt      960
cgtgtctctt aacaaccctc atgagaagac cttcaatcca atgtgcaagg atgtttgtga     1020
aacagcaaga ttcgaggaggca aacaacatga aaatcaaaat ttttccaatc acacagtggg     1080
attcaccatc tgttgtgaat taccagactt tcttggaac tcaaaagtta ttcttcctaa     1140
ggagtttcaa ggcaaaaact accgcaagtt gcttaaaatg ccaggaaagc cataaaaact     1200
ttcatcttat ggtgttgtca cacggcaata gttttgacaa cagatcctag ctcaaacgga     1260
attcaatagc attttccttt agaaaactat catattttca tcgaaaaaca gtctcttaca     1320
attctgagga tttttaaaaa agaatttcaa ttgaatcaga atctctttta agcactgaag     1380
agaatctcct gtcattttct gatcttctat gggctctttc cagaaaattc ttgattattc     1440
ctaagaagaa attgatattt agtgaagact gtaattgttt agcattcaac agtaaaaatt     1500
tgttgacaga gctataattc cgtgtgacaa caccattagt ggaagactca acaaatcgat     1560
aaaaaaaaatg atttcaaaat ggtataatag taaaaataaa aacctttccg gcaataaatt     1620
attcctttga ggatcacaat gtcctgaata ttcacacagt gactgagttt taagattatt     1680
ttactctcaa atcgtataat aaaggacaaa aaacatgcgt aaataaagaa atttgagta     1740
cgtaaaaaaa aaaaaaaaaa aaaaaaaaaa aa                                     1772

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<210> 63

<211> 249

<212> PRT

<213> Phlebotomus perniciosus

<400> 63

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Met Asn Asn Leu Leu Thr Phe Phe Gly Val Leu Cys Phe Leu Gly Phe
1           5              10              15

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Ala Asn Ser Leu Arg Phe Pro Arg Asp Pro Asp Gln Thr Arg Trp Ala
20 25 30

Glu Lys Thr Cys Leu Arg Glu Phe Ser Arg Ala Pro Pro Ser Leu Leu
35 40 45

Lys Lys Trp Gln Gln Leu Asp Phe Pro Asn Thr Asn Leu Thr His Cys
50 55 60

Phe Ile Lys Cys Phe Thr Ser Tyr Leu Gly Val Tyr Asn Asp Thr Thr
65 70 75 80

Lys Lys Phe Asn Val Asp Gly Ile Lys Thr Gln Phe Lys Ser Gln Glu
85 90 95

Ile Pro Ala Pro Gln Gly Leu Glu Thr Leu Arg Lys Thr Ser Lys Gly
100 105 110

Thr Cys Lys Asp Ile Tyr Leu Met Thr Val Asp Leu Val Lys Lys Asn
115 120 125

Lys Leu Gln Phe Ala Lys Ala Phe His Gly Ile Ser Ala Glu Ala Ala
130 135 140

Lys Trp Tyr Thr Gln His Lys Gly Asn Val Lys Gly Lys Tyr Gln Lys
145 150 155 160

Ala Ser Glu Phe Cys Lys Ser Lys Asp Asp Glu Cys Arg Leu His Cys
165 170 175

Arg Phe Tyr Tyr Tyr Arg Leu Val Asp Glu Asp Tyr Gln Ile Phe Asn
180 185 190

Arg Asn Leu Lys Ile Asn Gly Ile Ser Asn Ala Gln Leu Gln Gln Cys
195 200 205

Arg Asn Lys Ala Ser Gln Ala Lys Gly Cys Gln Val Ala Lys Val Leu
210 215 220

Arg Gln Cys Leu Lys Asp Ile Asn Pro Glu Asn Val Lys Ala Thr Leu
225 230 235 240

Lys Glu Leu Asp Glu Ile Ser Ala Lys
245

<210> 64
 <211> 952
 <212> DNA
 <213> *Phlebotomus perniciosus*

<400> 64
 ccattacggc cgaggagtct ctttcaacgc ttaatatcag caatgaataa cttgttaaca 60
 ttctttggag tactttgctt cttgggcttt gctaactctc tgcgattccc tcgtgaccca 120
 gaccaaacca gatgggcgga aaagacttgt ctgagagaat tttctcgtgc tccacctagt 180
 cttttaaaga aatggcaaca actggacttt cccaatacca atctcaccca ctgcttcac 240
 aagtgttca cttcgtatct tggagtctac aacgacacga ctaagaaatt taacgtggac 300
 ggaattaaaa cccaatttaa aagtcaggaa attcctgcac ctcaaggctt tgagacactt 360
 cgtaaaacat ctaaaggaac ctgcaaggat atttatctaa tgactgtgga ccttgtcaag 420
 aaaaacaagc tacaattcgc aaaagctttc catggaattt ctgcagaagc tgcaaaatgg 480
 tataccaac ataaaggaaa tgtaaggga aagtaccaga aagcatcgga attctgcaaa 540
 tctaaagatg atgagtgtag gctccattgc cgattctact actaccgctt agttgacgag 600
 gactaccaga tattcaacag aaatttaaaa atcaacggta tttccaacgc tcaacttcag 660
 caatgcagga acaaagccag tcaagctaag ggttgccagg tggcaaaggc cctaaggcaa 720
 tgtctcaaag acattaatcc tgaaaatgta aaagcgactt tgaaggagtt ggatgagata 780
 tcggcgaaat aatatactta aattaacccc atcagcccaa tttagcgtaa tttctcgacc 840
 gtagaaaaag gtgtttaact tacgggtgat tgagtgtgaa taatttagcg gctgtgggag 900
 atgaaatgac tattaaaagg tttatatccc caaaaaaaaa aaaaaaaaaa aa 952

<210> 65
 <211> 236
 <212> PRT
 <213> *Phlebotomus perniciosus*

<400> 65

Met Leu Gln Ile Lys His Phe Leu Phe Phe Val Val Leu Leu Val Ile
 1 5 10 15

Val His Ala Asn Asp Tyr Cys Gln Pro Lys Leu Cys Thr Asn Gly Lys
 20 25 30

Thr Val Lys Pro His Ile Gly Cys Arg Asn Asn Gly Asp Phe Asp Arg
 35 40 45

Ser Ala Cys Pro Asn Asp Ala Gln Met Val Glu Met Thr Gln Gln Arg
 50 55 60

Lys Glu Leu Phe Leu Lys Ile His Asn Arg Leu Arg Asp Arg Phe Ala
65 70 75 80

Arg Gly Ser Val Pro Asn Phe Lys Ser Ala Ala Lys Met Pro Met Leu
85 90 95

Lys Trp Asp Asn Glu Leu Ala Lys Leu Ala Glu Tyr Asn Val Arg Thr
100 105 110

Cys Lys Phe Ala His Asp Gln Cys Arg Ala Thr Thr Ala Cys Pro Tyr
115 120 125

Ala Gly Gln Asn Leu Gly Gln Met Leu Ser Ser Pro Asp Tyr Leu Asp
130 135 140

Pro Gly Tyr Ala Ile Lys Asn Ile Thr Arg Glu Trp Phe Leu Glu Tyr
145 150 155 160

Lys Trp Ala Asp Gln Gln Arg Thr Asn Thr Phe Thr Gly Gly Pro Gly
165 170 175

Lys Asp Gly Lys Gln Ile Gly His Phe Thr Ala Phe Val His Glu Lys
180 185 190

Ser Asp Lys Val Gly Cys Ala Val Ala Lys Leu Thr Asn Arg Gln Phe
195 200 205

Asn Met Lys Gln Tyr Leu Ile Ala Cys Asn Tyr Cys Tyr Thr Asn Met
210 215 220

Met Asn Glu Lys Ile Thr Ala Gln Val Pro Pro Phe
225 230 235

<210> 66

<211> 1033

<212> DNA

<213> Phlebotomus perniciosus

<400> 66

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ccgacatggt gcaaattaaa catttcttgt tctttgtggt gttactcgtg atcgttcacg 120

ctaacgacta ttgccagccg aaattgtgca caaatggcaa aacagtgaag cctcacattg 180

gatgcaggaa taatggagat ttcgatagaa gtgcctgtcc aaatgatgct cagatggttg 240

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aatgactca acagaggaag gagctctttc ttaagattca caatcgctt cgcgataggt      300
tcgctcgtgg ctcaagtccc aatttcaagt cagccgcaa gatgccaatg ctgaaatggg      360
acaatgaatt ggccaagttg gcagaataca atgtgagaac gtgcaaattt gctcacgatac      420
agtgtcgcgc aaccacagct tgtccttatg ctggtcagaa cttggggcaa atgttgtcat      480
ctccagatta tttggacccc ggctatgcca tcaagaatat caccaggag tggttcttg      540
agtataagtg ggcagatcaa caacgtacca acacctttac gggaggacct ggtaaagatg      600
gcaaacaaat tggtcacttt actgccttcg tccatgagaa gagcgacaag gttggatgtg      660
ctgttgctaa attaacgaac cgacaattca acatgaagca gtacctcatc gcttgcaact      720
actgctacac gaatatgatg aacgagaaga tcacagcaca ggtgcccccg ttctaagtgc      780
cagagtaaaa aatgcgattc caataacaag aatttgtgcg atgccagtga gaaagtcgaa      840
gccatcccag acatcttctt caagaagcgc aggacataat tctctgcttt cccatttgaa      900
aattgtaaaa taaatattgt tttcccttct atcaggtgaa ttggtgaaga tgagaagaaa      960
gaatgtataa gaaaataaga aataaacaga aactgagata tcgtaaaaaa aaaaaaaaaa     1020
aaaaaaaaaa aaa                                     1033

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<210> 67

<211> 257

<212> PRT

<213> *Phlebotomus perniciosus*

<400> 67

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Met Ile Val Lys Gly Leu Leu Gly Val Phe Leu Val Ile Leu Leu Val
1           5           10          15

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Cys Val Thr Glu Gln Gly Val Asp Gly Tyr His Arg Ala Asn Gly Asp
          20           25           30

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Tyr Gly Tyr Ser Tyr Glu Asn Arg His His Val Val Asn Gly Asp Glu
35           40           45

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Glu Glu His Glu Ile Lys His Thr Asn Ser Arg Lys Phe Asp Asp Asp
50           55           60

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Asp Tyr Leu Phe Ser His Gly Tyr Ala Ala Tyr Asp Asp Glu Asp Asp
65           70           75           80

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Glu Asp Glu Arg Gln Gly Tyr Ser Arg Gly Gly Gly Gly Ala Gly Asp
85           90           95

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Ser Ser Arg Asp Pro Gly Phe Tyr Arg Arg Gly Ser Gln Glu Gln Ser
 100 105 110

Tyr Asp Pro His Ser Gly Gln Thr Ala Pro Gly Tyr Ser Glu Ser Ser
 115 120 125

Glu Tyr Glu His Ser Gly Asp Tyr Asp Asn Ser Gln Asn Gln Gln Tyr
 130 135 140

Ser Ser Thr Pro Ser Asn Ala Asn Val Asn Leu Ile Asp Gln Tyr Leu
 145 150 155 160

His Leu Ile Gln Leu His Ser Ile Pro Ser Asp Leu Val Gln Tyr Ala
 165 170 175

Glu Ser Tyr Leu Thr His Ala Lys Asn Ser Ile Arg Tyr Tyr Ala Val
 180 185 190

His Ala Lys Asp Phe Glu Arg Ile Arg Pro Cys Leu Glu Ser Val Thr
 195 200 205

Lys Tyr Phe Asn Met Leu Asn Asp Asp Leu Ala Arg Glu Tyr Val Arg
 210 215 220

Cys Gln Arg Gln Cys Tyr Leu Asp Arg Leu Asn Ser Tyr Thr Thr Ala
 225 230 235 240

Ile Ser Gln Tyr Thr Val Thr Thr Asn Ala Cys Ile Asn Asn Arg Leu
 245 250 255

Asn

<210> 68
 <211> 934
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 68
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 gattgagaaa cgatgatcgt gaaggggtctc cttgggggtgt ttcttgtgat cttgctcgtg 120
 tgcgtagacag aacagggagt ggacggatac cacagggcta atgggggacta tggttacagc 180
 tacgaaaacc ggcatacagt agtcaacgga gatgaggagg aacatgaaat aaaacatact 240
 aactctcgta aatttgatga tgacgactat ctctttagtc acggctacgc cgcctacgac 300

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gacgaagacg atgaagatga acgacagggc tattcaaggg gcggtggggg agccggagac      360
agtagcagag atcccggtatt ttatcgtcgt ggaagtcagg aacaatctta cgatccccac      420
agcggtcaga cagctcctgg ctactcagaa tccagtgaat acgaacatag cggagactac      480
gataactccc agaaccagca atattcctca actccctcta acgctaacgt taacctaatc      540
gaccagtatc tccatctaata ccaattacat agcatcccat ccgatttagt ccaatacgcc      600
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tttgagagga ttcgaccctg ccttgaatcc gtcacgaagt atttcaatat gctcaatgac      720
gatctcgcca gggagtagct cagatgtcaa cgacaatgtt accttgatcg tctcaatagc      780
tacacaacgg ctatctctca gtatactgtc accacaaatg cctgcataaa caaccgtttg      840
aactgaagat gaggtttttt ttgtgaaata tttatttggg tcagtgaaaa taaattttca      900
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<210> 69

<211> 331

<212> PRT

<213> *Phlebotomus perniciosus*

<400> 69

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Met Ile Leu Lys Leu Cys Ala Ile Ala Val Leu Phe Phe Leu Ile Gly
1           5           10           15

```

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Asp Gly Glu Ala Ala Pro Arg Pro Thr Arg Phe Ile Pro Phe Ala Ile
20           25           30

```

```

Ile Ser Asp Leu His Arg Lys Ala Met His Asp Glu Lys Asn Arg Phe
35           40           45

```

```

Thr Ser Ile Val Lys Tyr Gly Gln Leu Lys Tyr Asn Gly Glu Lys Tyr
50           55           60

```

```

Thr Leu Ser Ile Arg Ser Glu Asn Leu His Tyr Phe Thr Lys Asp Thr
65           70           75           80

```

```

Tyr Lys Gly Thr Gly Ala Asp Met Ser Glu Leu Ile Tyr Phe Asn Asp
85           90           95

```

```

Lys Leu Tyr Thr Leu Asn Asp Glu Thr Gly Thr Ile Tyr Glu Val Lys
100          105          110

```

```

His Gly Gly Glu Leu Ile Pro Trp Ile Thr Leu Lys Asn Asp Asp Gly
115          120          125

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Asn Gln Lys Asp Gly Phe Lys Ala Lys Trp Ala Thr Val Lys Gly Asn
 130 135 140

Lys Leu Ile Val Gly Ser Ala Gly Met Ala Phe Leu Asp Ala Lys Thr
 145 150 155 160

Met Asn Ile Asp Arg Asp Ala Leu Trp Val Lys Glu Ile Ser Glu Ser
 165 170 175

Gly His Val Thr Asn Lys Tyr Trp Asp Ser Gln Tyr Lys Lys Val Arg
 180 185 190

Asp Ala Met Gly Leu Val Ser Gly Phe Val Trp His Glu Ala Val Asn
 195 200 205

Trp Ser Pro Arg Lys Asn Leu Trp Val Phe Met Pro Arg Lys Cys Thr
 210 215 220

Asn Glu Pro Tyr Thr Val Arg Leu Asp Lys Lys Thr Gly Cys Asn Gln
 225 230 235 240

Ile Ile Thr Ala Asn Glu Asn Phe Asn Asp Val Arg Ala Ile His Ile
 245 250 255

Asn Arg Ala Ala Ala Asp Pro Ala Ser Gly Phe Ser Ser Phe Lys Phe
 260 265 270

Ile Pro Asn Thr Arg Asn Asn Asp Ile Phe Ala Ile Lys Thr Ile Glu
 275 280 285

Arg Asn Gly Gln Thr Ala Thr Tyr Gly Thr Val Ile Asp Ile Asn Gly
 290 295 300

Lys Thr Leu Leu Pro Asp Gln Arg Ile Leu Asp Asp Lys Tyr Glu Gly
 305 310 315 320

Ile Ala Phe Phe Lys Asp Pro Lys Gly Ile Lys
 325 330

<210> 70

<211> 1102

<212> DNA

<213> Phlebotomus perniciosus

<400> 70

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ctatcatctc agatctgcac aggaaggcca tgcacgacga aaagaacaga tttactagta      180
tagtgaaata tgggtcaattg aagtacaatg gagagaaata tactctgtcc atcagaagtg      240
agaatctcca ttatttcaca aaggacacct acaaaggaac cggagccgat atgtccgagt      300
tgatctactt caatgacaag ctctacactc ttaacgacga aacaggaact atctatgagg      360
tgaaacacgg cggagagctc attccatgga taactctcaa gaatgacgat ggaaatcaaa      420
aggacggctt caaagctaaa tgggcaacag ttaagggtaa caagttgatt gtcggatcag      480
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caaggaagaa tctttgggtc ttcattgccc ggaaatgcac aaatgaacca tataccgttc      720
gcttagacaa gaaaaccgga tgcaatcaga ttatcacggc caatgaaaac ttcaatgatg      780
ttagagcaat tcatatcaat cgagccgctg cagatccagc ttctggattc tcctctttca      840
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gccaaacacg cacttatggc acagtgattg acatcaatgg gaagactttg ttgcccgatc      960
agcgaattct cgatgataaa tatgaaggaa ttgcattttt caaggatccc aaaggaatta    1020
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```

<210> 71
 <211> 230
 <212> PRT
 <213> *Phlebotomus perniciosus*

<400> 71

```

Met Asn Thr Leu Leu Lys Val Ala Val Leu Leu Ser Leu Gly Gly Thr
1           5           10          15

```

```

Gly Tyr Ser Trp Gln Tyr Pro Arg Asn Ala Asp Gln Thr Leu Trp Ala
20           25           30

```

```

Trp Arg Ser Cys Gln Lys Glu His Ile Gly Asp Asp Gln Ala Leu Leu
35           40           45

```

```

Lys Lys Trp Leu Lys Phe Glu Ile Pro Asp Asp Lys Val Thr His Cys
50           55           60

```

Phe Ile Lys Cys Thr Trp Ile His Leu Gly Met Tyr Asp Glu Lys Thr
65 70 75 80

Lys Thr Ile Arg Val Asp Lys Val Lys Gln Gln Phe Glu Gly Arg Lys
85 90 95

Leu Pro Val Pro Ala Glu Ile Ser Lys Leu Glu Gly Pro Thr Asp Gly
100 105 110

Asp Cys Glu Lys Ile Tyr Arg Lys Thr Lys Ala Phe Leu Asp Ala Gln
115 120 125

Met Lys Asn Tyr Arg Ile Ala Phe Tyr Gly Ile Tyr Asp Gly Ser Asp
130 135 140

Ala Trp Phe Ala Glu His Pro Glu Thr Lys Pro Lys Lys Thr Lys Ile
145 150 155 160

Ser Glu Phe Cys Lys Gly Arg Glu Gly Gly Lys Glu Gly Thr Cys Lys
165 170 175

His Ala Cys Ser Met Tyr Tyr Tyr Arg Leu Val Asp Glu Asp Asn Leu
180 185 190

Val Ile Pro Phe Arg Lys Leu Pro Gly Ile Ser Glu Ser Asp Leu Lys
195 200 205

Gln Cys Arg Asp Ala Ala Ser Lys Lys Ser Gly Cys Gln Val Ala Asp
210 215 220

Asp Asn Leu Arg Leu Ser
225 230

<210> 72

<211> 845

<212> DNA

<213> Phlebotomus perniciosus

<400> 72

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gatcgtgtca aaaggagcac atcggcgacg accaagcatt attgaagaaa tgggtgaaat 180

ttgaaattcc agatgataaa gtaacgcatt gttttattaa atgtacttgg atccatttag 240

gaatgtacga tgaaaaaact aaaaccatta gggttgataa ggtcaagcaa caattcgagg 300

gacgcaaatt accagttcct gctgaaatca gcaaattaga gggtcctaca gatggcgatt 360
 gtgaaaaaat ttacagaaaa actaaggctt ttcttgacgc tcaaatgaag aattatcgca 420
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 ttcccttcag gaagttgccca ggcattctcag agtctgatct taaacaatgc agagatgccg 660
 ctagcaagaa aagtggatgc caagttgctg atgacaatct acgattgtct taacaagatc 720
 aacccgacag gtcttaaaac tgctttaaat acgctcgatg agcaatcatt aacaaattat 780
 tagaaaagaa ataaaaattg atttcgagca atcgtaaaaa aaaaaaaaaa aaaaaaaaaa 840
 aaaaaa 845

<210> 73
 <211> 49
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 73

Met Lys Tyr Phe Ser Leu Asn Phe Leu Leu Ile Val Ile Leu Leu Ile
 1 5 10 15

Val Ala Cys Ser Pro Gln Leu Pro Cys Leu Pro Gln Asp Ser Lys Lys
 20 25 30

Lys Pro Ser Asn Pro Arg Pro Lys Leu Ser Ala Arg Ser Gly Leu Ser
 35 40 45

Tyr

<210> 74
 <211> 521
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 74
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 agaaaaagcc gtccaatcct cgtcctaaat tatcggccag aagtggtttg tcttattgag 180
 ttatcacact aggaattcga tgcagtaatt tattacgtgg gcattgtggc ttcatagctg 240
 gggccgtaaa aattaaaaga caaaaagaaa ttattacatg acggccgcca taagtcgacg 300

aaaatggaca taacatcctt gactacctat cgtaatgtga atttgaaaaa ttatacaaaa 360
 aaataattat gaattagcaa aaataaaaat tatcagagga gcagatctgc tgttatgatt 420
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 ttccaactgt gtcaaaaaaa aaaaaaaaaa aaaaaaaaaa a 521

<210> 75
 <211> 82
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 75

Met Lys Lys Ile Val Leu Phe Ser Phe Ile Phe Val Ala Leu Val Ile
 1 5 10 15

Ser Ala Lys Ala Ile Glu Thr Glu Leu Asp Asp Pro Asp Asp Ala Thr
 20 25 30

Lys Gly Arg Asp Val Ala Lys Ala Glu Pro Gly Gln Leu Gly Gln Val
 35 40 45

Pro Val Val Pro Asp Leu Asn Pro Ser Asn Thr Arg Lys Arg Arg Asn
 50 55 60

Arg Ser Arg Lys Arg Arg Arg Asn Leu Gly Lys Arg Leu Lys Lys Val
 65 70 75 80

Phe Ala

<210> 76
 <211> 379
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 76
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 gtcgggatgt tgcaaggca gaacctggac aactgggaca agttccagtt gtacctgatt 180
 taaatccttc gaacacgagg aaacggagga atagatccag aaaaaggcga cgaaatctag 240
 gaaagagact caaaaaagtt ttgcataga aattaatact aaaaagatta aaactatgtc 300
 aatttgatgc cttttgagca ttcaattaaa agtatgaca aattattaag aaaaaaaaaa 360
 aaaaaaaaaa aaaaaaaaaa 379

<210> 77
 <211> 293
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 77

Met Met Ser Arg Trp Ser Lys Ser Val Lys Phe Val Cys Leu Leu Leu
 1 5 10 15

Cys Gly Gly Phe Thr Phe Leu Thr Thr Ser Ala Arg Ala Lys Pro Thr
 20 25 30

Leu Thr Phe Gln Leu Pro Pro Ala Leu Thr Asn Leu Pro Pro Phe Ile
 35 40 45

Gly Ile Ser Arg Phe Val Glu Arg Lys Met Gln Asn Asp Gln Met Lys
 50 55 60

Thr Tyr Thr Gly Val Arg Gln Thr Asn Asp Ser Leu Val Met Ile Tyr
 65 70 75 80

His His Asp Leu Thr Ile Ala Ile Val Glu Leu Gly Pro Glu Lys Thr
 85 90 95

Leu Leu Gly Cys Glu Leu Ile Glu Ile Asn Asn Asp Asp Glu Gly Ala
 100 105 110

Lys Val Leu Thr Glu Leu Ala Thr Val Asn Ile Pro Leu Gln Ile Asp
 115 120 125

Phe Arg Glu Met Val Lys Leu Met Lys Gln Cys Glu Lys Ile Asp Tyr
 130 135 140

Met Arg Lys Val Lys Arg Gln Gly Ala Ser Glu Ser Asp Gln Thr Thr
 145 150 155 160

Asn Arg Gln His Gln Thr Gly Tyr Phe Gly Leu Gly Gly Ala Thr Ala
 165 170 175

Gly Leu Ser Ile Leu Ser Gly Ile Leu Pro Gly Thr Lys Trp Cys Gly
 180 185 190

Thr Gly Asp Ile Ala Lys Thr Tyr His Asp Leu Gly Thr Glu Ala Thr
 195 200 205

Met Asp Met Cys Cys Arg Thr His Asp Leu Cys Pro Val Lys Val Arg
 210 215 220

Ser Tyr Gln Gln Arg Tyr Asn Leu Ser Asn Asn Ser Ile Tyr Thr Lys
 225 230 235 240

Ser Pro Cys Lys Cys Asp Asp Met Leu Phe Asn Cys Leu Lys Arg Thr
 245 250 255

Asn Thr Ser Ala Ser Gln Phe Met Gly Thr Ile Tyr Phe Asn Val Val
 260 265 270

Gln Val Pro Cys Val Leu Asp Thr Glu Arg Gly Tyr Arg Phe Arg Lys
 275 280 285

Ala Arg Thr Phe Ser
 290

<210> 78
 <211> 1613
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 78
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 aagggtgcaat agagatacta aactagagga aagacttgaa cgggtgacaga ggaataggag 240
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 aagagttttc tacacagaga aattgcgagg tcacttattg gaaatcaatg agaaagtttt 360
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 cttttctgtg gagagacgat aaaaggaaat tcgatattta tgggaaaagt gatgaattag 480
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 cactggcggt cggcagacga acgactctct cgtgatgatc taccaccatg atctgacgat 840
 cgccatcgtg gaattgggac cagagaagac tctcttgggt tgtgaattga tagaaattaa 900

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gaaagtgaaa cgccagggag catcagagag tgaccagaca acaaatcgtc aacatcagac    1080
gggctacttt ggactcggag gcgccaccgc cggcttaagc atcctcagtg gcatccttcc    1140
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tcagcagcgc tacaatctca gcaataactc tatctacaca aaatctccct gcaaattgtga    1320
tgacatgctg ttcaattgcc tcaagaggac caacacgtca gcctcgcaat tcatggggac    1380
catctacttc aacgtgggtcc aagtgccatg tgttctggac acagagagag gctacagatt    1440
cagaaaagcg agaaccttct cctgagtatt gcaaaacaac gaaatctgcg gatttttttt    1500
tatttttggg acttttctgt tgtaaagacc atttcttgtg attttcagct gcggtgctct    1560
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<210> 79

<211> 137

<212> PRT

<213> *Phlebotomus perniciosus*

<400> 79

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Met Lys Gln Leu Val Val Phe Leu Ala Leu Ile Val Leu Ile Val Ile
1              5              10              15

```

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Cys His Ala Lys Arg Pro Ser Arg Lys Cys Arg Ser Gly Met Val Lys
20              25              30

```

```

Glu Glu Glu Cys Ile Leu His Cys Glu Tyr Lys Tyr Tyr Gly Phe Thr
35              40              45

```

```

Asp Asp Lys Phe Gln Leu Asp Ala Asp Gln Arg Gly Asn Phe Arg Phe
50              55              60

```

```

Ala Met Met Asp Tyr Gly Ala Ile Arg Met Asp Gln Glu Gly Gln Met
65              70              75              80

```

```

Asp Glu His Leu Lys Lys Cys Ala Asn Glu Ala Glu Lys Ala Pro Val
85              90              95

```

```

Cys Ser Lys Val Asp Lys Cys Arg Lys Ile Ile Gln Tyr Tyr Arg Cys
100             105             110

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Ala Val Asn Asn Lys Leu Phe Gln Tyr Asn Ala Tyr Ala Lys Ala Ile
 115 120 125

Ile Ala Leu Asp Lys Thr Ile Asn Val
 130 135

<210> 80
 <211> 518
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 80
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 cagtgtgctc caaggtggat aagtgtagga aaatcattca gtactatcgc tgtgcagtga 360
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<210> 81
 <211> 141
 <212> PRT
 <213> Phlebotomus perniciosus

<400> 81

Met Lys Gln Leu Pro Val Ile Leu Leu Ala Leu Val Phe Leu Ile Ala
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Lys Cys Arg Ser Glu Lys Pro Glu Tyr Lys Cys Arg Arg Asp Phe Lys
 20 25 30

Thr Glu Asp Lys Asn Cys Phe Leu Ser Cys Thr Phe Lys Asn Tyr His
 35 40 45

Phe Ile Asp Asn Lys Phe Arg Ile Glu Arg Lys Asn Ile Glu Asn Tyr
 50 55 60

Lys Lys Phe Ile Thr Asp Tyr Lys Ala Leu Lys Pro Asn Val Ser Asp
 65 70 75 80

Asn Asp Leu Glu Lys His Leu Leu Asp Cys Trp Asp Lys Phe Gln Lys
85 90 95

Ser Pro Glu Ala Ser Thr Arg Pro Glu Lys Cys Glu Lys Val Asn Asn
100 105 110

Phe Glu Arg Cys Val Ile Asp Lys Asn Ile Phe Asp Tyr Pro Ile Tyr
115 120 125

Phe Asn Ala Leu Lys Lys Ile Asn Tyr Ile Thr Lys Val
130 135 140

<210> 82

<211> 526

<212> DNA

<213> Phlebotomus perniciosus

<400> 82

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gaccgaggat aaaaattgct tcctttcttg tacattttaa aattaccact tcattgataa 180
caagttcagg attgaaagga agaattatga aaactacaag aagttcataa ctgactataa 240
ggccctgaaa cccaatgtta gcgataatga tttggaaaaa cacctggttg attggtggga 300
taaattccaa aaatcacctg aagcatcaac aaggcccgaa aaatgtgaaa aagtcaacaa 360
ctttgaaaga tgtgttattg acaagaatat ctttgattat cctatttact tcaatgcttt 420
gaagaaaata aattacatta caaaggttta atgaaaaatt gatgaaataa acataatgaa 480
ttattgcatt gaataacaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 526

<210> 83

<211> 97

<212> PRT

<213> Phlebotomus perniciosus

<400> 83

Met Lys Lys Ile Val Leu Phe Ser Val Ile Phe Ile Ala Leu Val Ile
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Ser Ala Lys Ala Ile Glu Asp Glu Asp Asp Asp Asp Asp Asp Glu
20 25 30

Ser Glu Asp Arg Asp Val Ala Arg Ala Glu Arg Glu Gln Gln Glu Glu
35 40 45

Glu Pro Asp Glu Pro Glu Tyr Ile Pro Ser Arg Pro Arg Asn Arg Ser
 50 55 60

Lys Met Arg Lys Trp Arg Asn Arg Asn Tyr Arg Lys Tyr Arg Asp Glu
 65 70 75 80

Ser Arg Lys Arg Lys Arg Asp Met Val Leu Asp Val Ile Arg Arg Phe
 85 90 95

Leu

<210> 84
 <211> 425
 <212> DNA
 <213> Phlebotomus perniciosus

<400> 84
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 tcgggatgtt gcgagggcag aacgtgaaca acaggaagaa gaaccagacg aacctgaata 180
 tattccttct agaccgagga atcggtcgaa aatgagaaaa tggaggaata gaaactatag 240
 aaaatataga gacgaaagta ggaaaagaaa gcgagatatg gttttggatg ttatcagaag 300
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 aaaaa 425

<210> 85
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide primer.

<400> 85
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<210> 86
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide primer.

<400> 86
ctcttcgcta ttacgccagc tg

22

<210> 87
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer.

<400> 87
tctcgggaag cgcgccattg tggt

24

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
1 April 2004 (01.04.2004)

PCT

(10) International Publication Number
WO 2004/027041 A3

(51) International Patent Classification⁷: **A61K 38/00**,
39/00, 39/38, C07K 16/00, C07H 21/02, 21/04

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(21) International Application Number:
PCT/US2003/029833

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(22) International Filing Date:
18 September 2003 (18.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/412,327 19 September 2002 (19.09.2002) US
60/425,852 12 November 2002 (12.11.2002) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Declaration under Rule 4.17:

— of inventorship (*Rule 4.17(iv)*) for US only

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
24 February 2005

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: *P. ARIASI* POLYPEPTIDES, *P. PERNICIOSUS* POLYPEPTIDES AND METHODS OF USE

(57) Abstract: Substantially purified salivary *P. ariasi* and *P. perniciosus* polypeptides, and polynucleotides encoding these polypep-
tides are disclosed. Vectors and host cells including the *P. ariasi* and *P. perniciosus* polynucleotides are also disclosed. In one em-
bodiment, a method is disclosed for inducing an immune response to sand fly saliva. In other embodiments, methods for treating or
preventing *Leishmaniasis* are disclosed.

WO 2004/027041 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/29833

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00, 39/00, 39/38; C07K 16/00; C07H 21/02, 21/04
US CL : 424/184.1, 185.1; 530/300, 350; 536/23.1;

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/184.1, 185.1; 530/300, 350; 536/23.1;

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y — A	SAMBROOK et al. Molecular Cloning A Laboratory Manual. Second Edition. Cold Spring Harbor Laboratory Press. 1989, Vol. 3, pages 16.2 to 16.81, see entire document.	13-20 3, 4, 9, 10
Y X — Y	CAMPBELL, A. M. Monoclonal Antibody Technology. New York: Elsevier Science Publishing Company, Inc. 1984, pages 1-32, see in particular page 29, section 1.3.4. Database A Genseq 29 January 2004. Accession Number ABB71995. 26 March 2002, residues 671-682 are 100% identical to residues 385-396 of SEQ ID NO:1.	25-38 1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A Genseq 29 January 2004. Accession Number ABG718028. 18 February 2002, residues 254-261 are 100% identical to residues 141-148 of SEQ ID NO:3.	1, 2, 5-8, 11, 12 13-20, 25-38



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

07 October 2004 (07.10.2004)

Date of mailing of the international search report

04 JAN 2005

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	Database SPTreMBL. Accession Number Q95WD8. 19 December March 2001, residues 253-261 are 100% identical to residues 243-251 of SEQ ID NO:5 and residues 240-261 are 100% identical to residues 244-252 of SEQ ID NO:7.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database SPTreMBL. Accession Number Q23404. 06 June 1998, residues 190-197 are 100% identical to residues 505-515 of SEQ ID NO:9.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number AAG03191. 06 October 2000, residues 91-98 are 100% identical to residues 1-8 of SEQ ID NO:11.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number ABG24332. 18 February 2002, residues 6-13 are 100% identical to residues 234-241 of SEQ ID NO:13.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database SPTreMBL. Accession Number Q9HNC7. 16 March 2001, residues 93-100 are 100% identical to residues 8-15 of SEQ ID NO:15.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number AAU48010. 27 February 2002, residues 105-112 are 100% identical to residues 61-68 of SEQ ID NO:17.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database SPTreMBL. Accession Number Q95WE2. 01 December 2001, residues 24-34 are 100% identical to residues 23-33 of SEQ ID NO:19.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database PIR_78. Accession Number G81431. 31 March 2000, residues 6-13 are 100% identical to residues 8-15 of SEQ ID NO:21.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database SPTreMBL. Accession Number Q9XZ44. 12 November 1999, residues 105-118 are 100% identical to residues 107-120 of SEQ ID NO:23.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number AAB94843. 26 June 2001, residues 319-326 are 100% identical to residues 5-12 of SEQ ID NO:25.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number ABB61398. 26 March 2002, residues 225-234-682 are 100% identical to residues 133-142 of SEQ ID NO:27.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number AAB42952. 08 February 2001, residues 259-270 are 100% identical to residues 23-34 of SEQ ID NO:29.	1, 2, 5-8, 11, 12 13-20, 25-38

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	Database SPTreMBL. Accession Number Q9RVD4. 01 May 2000, residues 62-69 are 100 % identical to residues 148-155 of SEQ ID NO:31.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database SPTreMBL. Accession Number Q95WE2. 01 December 2001, residues 181-190 are 100 % identical to residues 178-187 of SEQ ID NO:33.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database PIR_78. Accession Number B64020. 10 September 1999, residues 10-17 are 100 % identical to residues 10-17 of SEQ ID NO:35.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number ABB57882. 26 March 2002, residues 477-486 are 100 % identical to residues 119-128 of SEQ ID NO:37.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database PIR_78. Accession Number T50116. 09 June 2000, residues 219-226 are 100 % identical to residues 10-17 of SEQ ID NO:39.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database PIR_78. Accession Number F90270. 24 May 2001, residues 372-380 are 100 % identical to residues 53-61 of SEQ ID NO:41.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number ABB58845. 26 March 2002, residues 207-217 are 100 % identical to residues 185-195 of SEQ ID NO:43.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database A_Genseq_29 January 2004. Accession Number AAB83185. 09 July 2001, residues 99-106 are 100 % identical to residues 89-96 of SEQ ID NO:45.	1, 2, 5-8, 11, 12 13-20, 25-38
X — Y	Database Swissprot_42. Accession Number Q57124. 10 November 1997, residues 346-353 are 100 % identical to residues 9-16 of SEQ ID NO:47.	1, 2, 5-8, 11, 12 13-20, 25-38

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International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-20 and 25-38

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claim(s) 1-20 and 25-38, drawn to *P. ariasi* salivary polypeptides, nucleic acids, vectors, host cells and methods.

Group II, claim(s) 21-24, drawn to antibodies that bind *P. ariasi* salivary polypeptides.

Group III, claim(s) 39-58 and 64-76, drawn to *P. perniciosus* salivary polypeptides, nucleic acids, vectors, host cells and methods.

Group IV, claim(s) 59-62, drawn to antibodies that bind *P. perniciosus* salivary polypeptides.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

The antibodies of Group II that bind different polypeptides of Group I:

SEQ ID NO:1,
SEQ ID NO:3,
SEQ ID NO:5,
SEQ ID NO:7,
SEQ ID NO:9,
SEQ ID NO:11,
SEQ ID NO:13,
SEQ ID NO:15,
SEQ ID NO:17,
SEQ ID NO:19,
SEQ ID NO:21,
SEQ ID NO:23,
SEQ ID NO:25,
SEQ ID NO:27,
SEQ ID NO:29,
SEQ ID NO:31,
SEQ ID NO:33,
SEQ ID NO:35,
SEQ ID NO:37,
SEQ ID NO:39,
SEQ ID NO:41,
SEQ ID NO:43,
SEQ ID NO:45, and
SEQ ID NO:47.

The polypeptides and nucleic acids of Group III as follows:

SEQ ID NO:49,
SEQ ID NO:51,
SEQ ID NO:53,
SEQ ID NO:55,
SEQ ID NO:57,
SEQ ID NO:59,
SEQ ID NO:61,
SEQ ID NO:63,
SEQ ID NO:65,
SEQ ID NO:67,
SEQ ID NO:69,
SEQ ID NO:71,
SEQ ID NO:73.

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SEQ ID NO:75,
SEQ ID NO:77,
SEQ ID NO:79,
SEQ ID NO:81, and
SEQ ID NO:83.

The antibodies of Group IV that bind different polypeptides of Group III:

SEQ ID NO:49,
SEQ ID NO:51,
SEQ ID NO:53,
SEQ ID NO:55,
SEQ ID NO:57,
SEQ ID NO:59,
SEQ ID NO:61,
SEQ ID NO:63,
SEQ ID NO:65,
SEQ ID NO:67,
SEQ ID NO:69,
SEQ ID NO:71,
SEQ ID NO:73,
SEQ ID NO:75,
SEQ ID NO:77,
SEQ ID NO:79,
SEQ ID NO:81, and
SEQ ID NO:83.

Continuation of B. FIELDS SEARCHED Item 3:

DIALOG, WEST, EMBASE, COMMERICAL SEQUENCE DATABASES.

SEARCH TERMS: P. araisi, saliva, salivary, polypeptide, peptide, antigen, isolate, purify, SEQ ID NOS:1-47.